Baskar, P
09/541873

Str.

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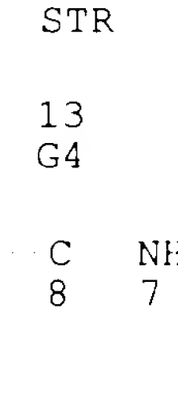

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VAR G3=O/S/NH
REP G4=(6-6) C
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STEREO ATTRIBUTES: NONE
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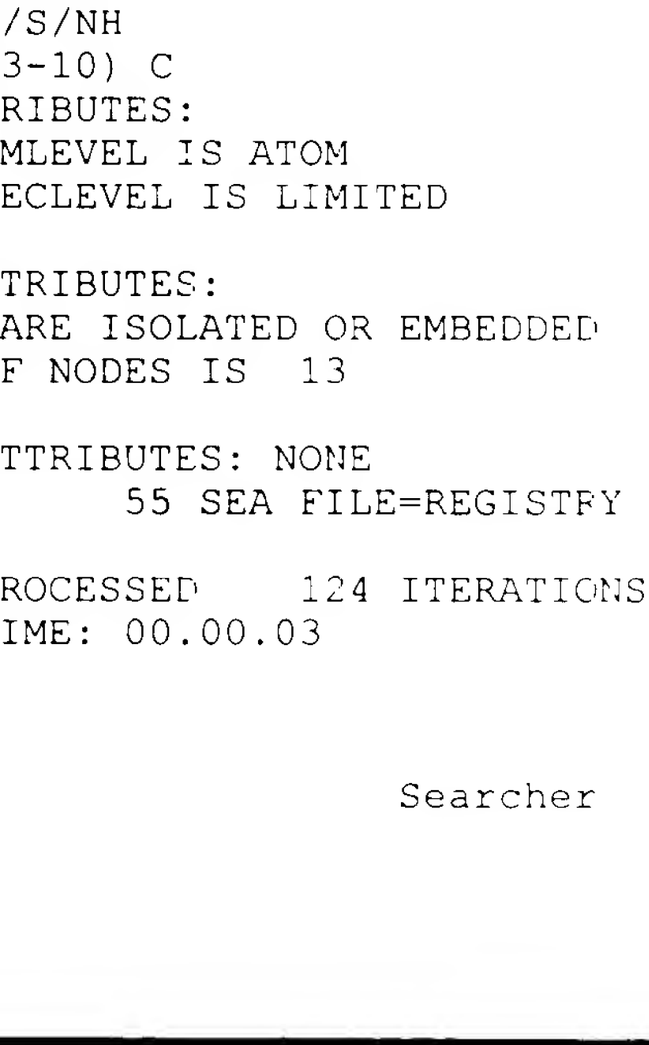

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VAR G2=O/S/NH
VAR G3=O/S/NH
VAR G4=O/S/NH
REP G5=(3-10) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.03

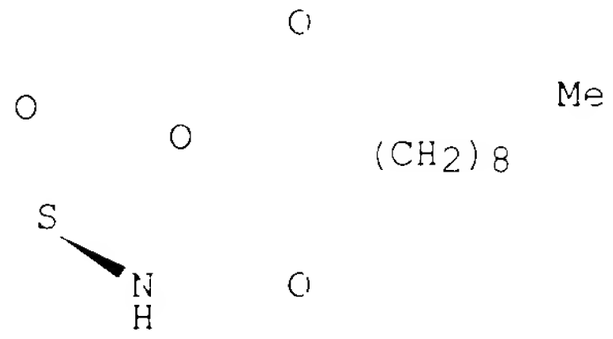
Searcher : Shears 308-4994

FILE 'HCAPLUS' ENTERED AT 14:30:56 ON 22 NOV 2002
L22 97 S L17
L23 47 S L22 AND AERUGINOS?

E1 THROUGH E20 ASSIGNED

L23 ANSWER 1 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:659402 HCAPLUS
TITLE: The Pseudomonas autoinducer N-(3-oxododecanoyl) homoserine lactone induces cyclooxygenase-2 and prostaglandin E2 production in human lung fibroblasts: implications for inflammation
AUTHOR(S): Smith, Roger S.; Kelly, Rodney; Iglewski, Barbara H.; Phipps, Richard P.
CORPORATE SOURCE: Departments of Microbiology and Immunology, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Immunology (2002), 169(5), 2636-2642
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pseudomonas **aeruginosa** causes lethal lung infections in immunocompromised individuals such as those with cystic fibrosis. The lethality of these infections is directly assocd. with inflammation and lung tissue destruction. P. **aeruginosa** produces several acylated homoserine lactones (AHL) that are important in the regulation of bacterial virulence factors. Little is known about the effects of AHLs on human cells. In this work we report that the AHL N-(3-oxododecanoyl) homoserine lactone (3O-C12-HSL) from P. **aeruginosa** induces cyclooxygenase (Cox)-2, a seminal proinflammatory enzyme. When primary normal human lung fibroblasts were exposed to 3O-C12-HSL, an 8-fold induction in mRNA and a 35-fold increase in protein for Cox-2 were obsd. In contrast, there was no substantial change in the expression of Cox-1. We also demonstrated that the induction of Cox-2 was regulated by 3O-C12-HSL activation of the transcription factor NF-.kappa.B. 3O-C12-HSL also stimulated an increase in the newly discovered inducible membrane-assocd. PGE synthase but had no effect on the expression of the cytosolic PGE synthase. We also demonstrate that 3O-C12-HSL stimulated the prodn. of PGE2. PGE2 is known to induce mucus secretion, vasodilation, and edema, and acts as an immunomodulatory lipid mediator. We propose that 3O-C12-HSL induction of Cox-2, membrane-assocd. PGE synthase, and PGE2 likely contributes to the inflammation and lung pathol. induced by P. **aeruginosa** infections in the lung. These studies further reinforce the concept that bacterial AHLs not only regulate bacterial virulence but also stimulate the activities of eukaryotic cells important for inflammation and immune defenses.
IT **168982-69-2**, n-(3-Oxododecanoyl) homoserine lactone
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(Pseudomonas autoinducer N-(3-oxododecanoyl) homoserine lactone induces cyclooxygenase-2 and prostaglandin E2 prodn. in human lung fibroblasts: implications for inflammation)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

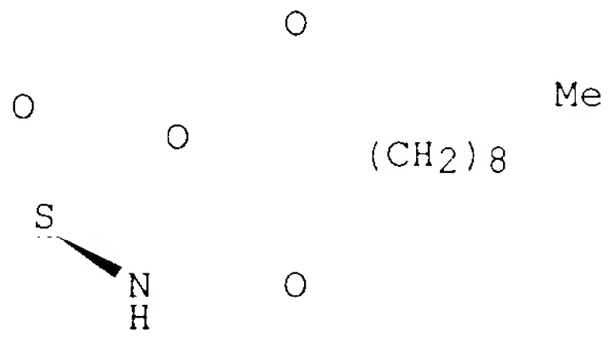
L23 ANSWER 2 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:629412 HCAPLUS
DOCUMENT NUMBER: 137:306278
TITLE: LasR, a transcriptional activator of Pseudomonas **aeruginosa** virulence genes, functions as a multimer
AUTHOR(S): Kiratisin, Pattarachai; Tucker, Kenneth D.; Passador, Luciano
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Journal of Bacteriology (2002), 184(17), 4912-4919
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Pseudomonas **aeruginosa** LasR protein functions in concert with N-3-oxo-dodecanoyl-L-homoserine lactone (3O-C12-HSL) to coordinate the expression of target genes, including many genes that encode virulence factors, with cell d. We used a LexA-based protein interaction assay to demonstrate that LasR forms multimers only when 3O-C12-HSL is present. A series of LasR mols. contg. internal deletions or substitutions in single, conserved amino acid residues indicated that the N-terminal portion of LasR is required for multimerization. Studies performed with these mutant versions of LasR demonstrated that the ability of LasR to multimerize correlates with its ability to function as a transcriptional activator of lasI, a gene known to be tightly regulated by the LasR-3O-C12-HSL regulatory system. A LasR mol. that carries a C-terminal deletion can function as a dominant-neg. mutant in P. **aeruginosa**, as shown by its ability to decrease expression of lasB, another LasR-3O-C12-HSL target gene. Taken together, our data strongly support the hypothesis that LasR functions as a multimer in vivo.

IT **168982-69-2**, N-3-Oxo-dodecanoyl-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LasR transcriptional activator can form multimer in presence of N-3-oxo-dodecanoyl-L-homoserine lactone)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:403802 HCAPLUS
DOCUMENT NUMBER: 136:400592
TITLE: Immunogenic conjugates comprising autoinducer and lysine-contg. protein as vaccine and for raising antibody to treat and diagnose Gram-neg. bacterial infection
INVENTOR(S): Kende, Andrew S.; Iglewski, Barbara H.; Smith, Roger; Phipps, Richard P.; Pearson, James P.
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

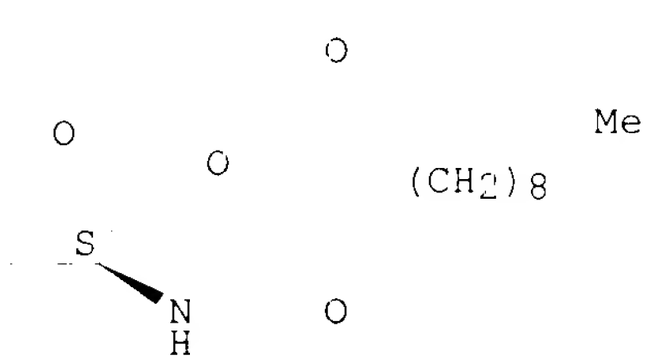
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6395282	B1	20020528	US 1999-293687	19990416

PRIORITY APPLN. INFO.: US 1998-82025P P 19980416
OTHER SOURCE(S): MARPAT 136:400592

AB The present invention relates to an immunogenic conjugate comprising a carrier mol. coupled to an autoinducer of a Gram neg. bacteria. The autoinducer is N-(3-oxododecanoyl)-L-homoserine lactone, N-(butanoyl)-L-homoserine lactone, N-hexanoyl-homoserine lactone, N-(3-oxohexanoyl)-homoserine lactone, N-.beta.-(hydroxybutyryl)-homoserine lactone, N-(3-oxooctanoyl)-L-homoserine lactone, or N-(3R-hydroxy-cis-tetradecanoyl)-L-homoserine lactone. The carrier mol. is bovine serum albumin, chicken egg ovalbumin, limpet hemocyanin, tetanus toxoid, diphtheria toxoid and thyroglobulin. The immunogenic conjugate, when combined with a pharmaceutically acceptable carrier, forms a suitable vaccine for mammals to prevent infection by the Gram neg. bacteria. The immunogenic conjugate is also used to raise and subsequently isolate antibodies or binding portions thereof which are capable of recognizing and binding to the autoinducer. The antibodies or binding portions thereof are utilized in a method of treating infections, a method of inhibiting autoinducer activity, and in diagnostic assays which detect the presence of autoinducers or autoinducer antagonists in fluid or tissue samples.

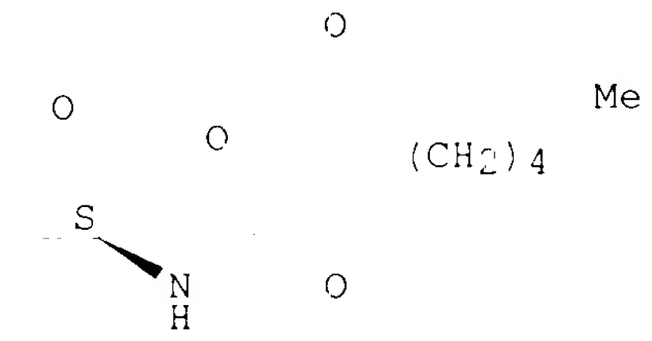
IT **168982-69-2P**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(immunogenic conjugates comprising autoinducer and lysine-contg. protein as vaccine and for raising antibody to treat and diagnose Gram-neg. bacterial infection)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



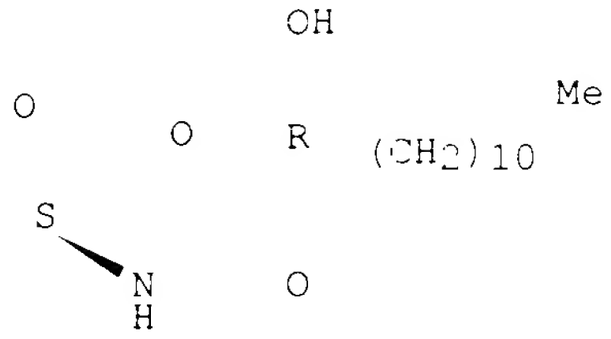
IT **147795-39-9P**, N-(3-Oxooctanoyl)-L-homoserine lactone
429675-20-7P
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(immunogenic conjugates comprising autoinducer and lysine-contg. protein as vaccine and for raising antibody to treat and diagnose Gram-neg. bacterial infection)
RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 429675-20-7 HCAPLUS
CN Tetradecanamide, 3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]-, (3R)- (9CI) (CA INDEX NAME)

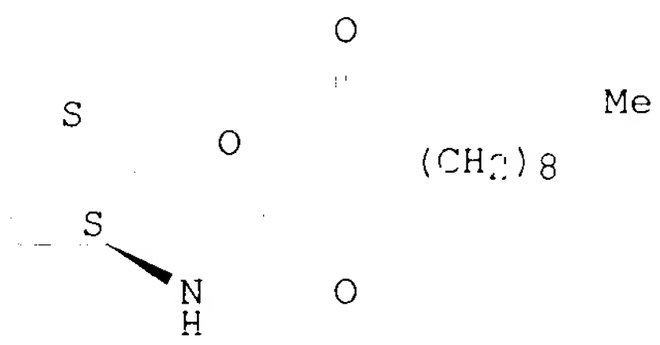
Absolute stereochemistry.



IT **177158-29-1P 182359-64-4P 216596-73-5P**
429675-30-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(immunogenic conjugates comprising autoinducer and lysine-contg. protein as vaccine and for raising antibody to treat and diagnose Gram-neg. bacterial infection)

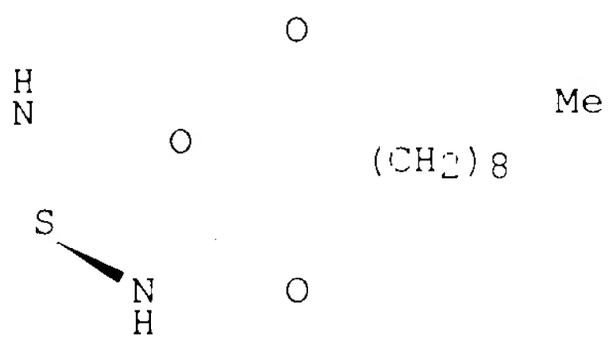
RN 177158-29-1 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-thienyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



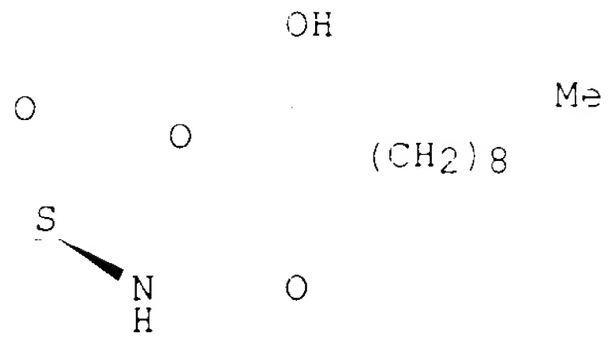
RN 182359-64-4 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-2-oxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 216596-73-5 HCAPLUS
CN Dodecanamide, 3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 429675-30-9 HCAPLUS
CN 6-Dodecenamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]-, (6E)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
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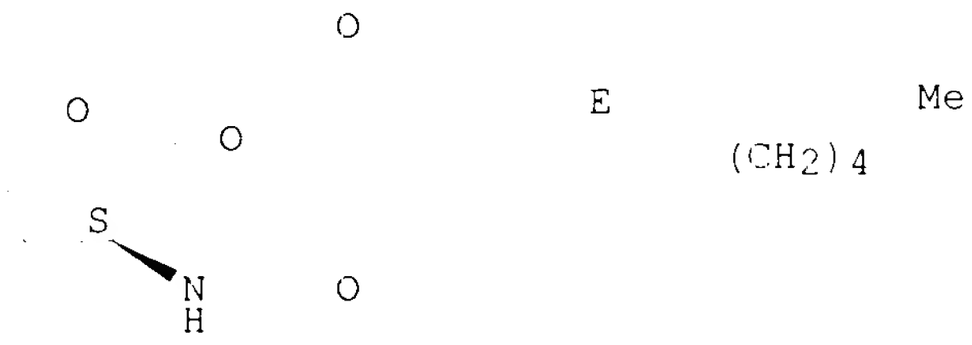


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:335966 HCAPLUS
DOCUMENT NUMBER: 137:307141
TITLE: Advancing the quorum in Pseudomonas **aeruginosa**: MvaT and the regulation of N-acylhomoserine lactone production and virulence gene expression
AUTHOR(S): Diggle, Stephen P.; Winzer, Klaus; Lazdunski, Andree; Williams, Paul; Camara, Miguel
CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Journal of Bacteriology (2002), 184(10), 2576-2586
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pseudomonas **aeruginosa** regulates the prodn. of many exoproteins and secondary metabolites via a hierarchical quorum-sensing cascade through LasR and RhlR and their cognate signal mols. N-(3-oxododecanoyl)-L-homoserine lactone (3O-C12-HSL) and N-(butanoyl)-L-homoserine lactone (C4-HSL). In this study, we found that transcription of the quorum sensing-regulated genes lecA (coding for PA-IL lectin), lasB (coding for elastase), and rpoS appeared to be growth phase dependent and their expression could not be advanced to the logarithmic phase in cells growing in batch

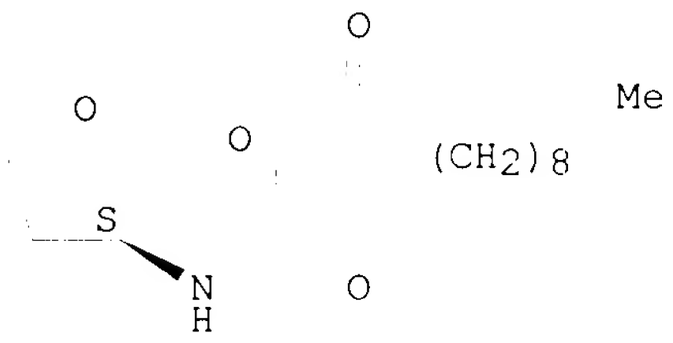
culture by the addn. of exogenous C4-HSL and 3O-C12-HSL. To identify novel regulators responsible for this growth phase dependency, a P. **aeruginosa** lecA::lux reporter strain was subjected to random transposon mutagenesis. A no. of mutants affected in lecA expression were found that exhibited altered prodn. of multiple quorum sensing-dependent phenotypes. While some mutations were mapped to new loci such as clpA and mvaT and a putative efflux system, a no. of mutations were also mapped to known regulators such as lasR, rhlR, and rpoS. MvaT was identified as a novel global regulator of virulence gene expression, as a mutation in mvaT resulted in enhanced lecA expression and pyocyanin prodn. This mutant also showed altered swarming ability and prodn. of the LasB and LasA proteases, 3O-C12-HSL, and C4-HSL. Furthermore, addn. of exogenous 3O-C12-HSL and C4-HSL to the mvaT mutant significantly advanced lecA expression, suggesting that MvaT is involved in the growth phase-dependent regulation of the lecA gene.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Pseudomonas **aeruginosa** MvaT and the regulation of N-acylhomoserine lactone prodn. and virulence gene expression)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:323501 HCAPLUS
DOCUMENT NUMBER: 137:75804
TITLE: Genetically programmed autoinducer destruction reduces virulence gene expression and swarming motility in Pseudomonas **aeruginosa** PAO1
AUTHOR(S): Reimmann, Cornelia; Ginet, Nathalie; Michel, Laurent; Keel, Christoph; Michaux, Patrick; Krishnapillai, Viji; Zala, Marcello; Heurlier, Karin; Triandafillu, Karine; Harms, Hauke; Defago, Genevieve; Haas, Dieter
CORPORATE SOURCE: Laboratoire de Biologie Microbienne, Universite de Lausanne, Lausanne, CH-1015, Switz.
SOURCE: Microbiology (Reading, United Kingdom) (2002), 148(4), 923-932
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology

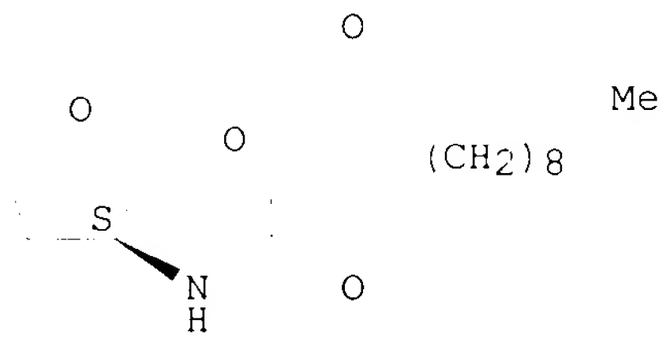
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Virulence in the opportunistic human pathogen P. **aeruginosa** is controlled by cell d. via diffusible signalling mols. ("autoinducers") of the N-acylhomoserine lactone (AHL) type. Two Bacillus sp. isolates (A23 and A24) with AHL-degrading activity were identified among a large collection of rhizosphere bacteria. From isolate A24 a gene was cloned which was similar to the aiiA gene, encoding an AHL lactonase in another Bacillus strain. Expression of the aiiA homolog from isolate A24 in P. **aeruginosa** PAO1 reduced the amt. of the quorum sensing signal N-oxododecanoyl-L-homoserine lactone and completely prevented the accumulation of the 2nd AHL signal, N-butyryl-L-homoserine lactone. This strongly reduced AHL content correlated with a markedly decreased expression and prodn. of several virulence factors and cytotoxic compds. such as elastase, rhamnolipids, HCN, and pyocyanin, and strongly reduced swarming. However, no effect was obsd. on flagellar swimming or on twitching motility, and aiiA expression did not affect bacterial adhesion to a polyvinylchloride surface. In conclusion, introduction of an AHL degrdn. gene into P. **aeruginosa** could block cell-cell communication and exoproduct formation, but failed to interfere with surface colonization.

IT **168982-69-2**
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(genetically programmed autoinducer destruction reduces virulence gene expression and swarming motility in Pseudomonas **aeruginosa** PAO1)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:239530 HCAPLUS
DOCUMENT NUMBER: 136:399636
TITLE: Pseudomonas **aeruginosa** quorum-sensing systems may control virulence factor expression in the lungs of patients with cystic fibrosis
AUTHOR(S): Erickson, David L.; Endersby, Ryan; Kirkham, Amanda; Stuber, Kent; Vollman, Dolina D.; Rabin, Harvey R.; Mitchell, Ian; Storey, Douglas G.
CORPORATE SOURCE: Department of Biological Sciences, University of

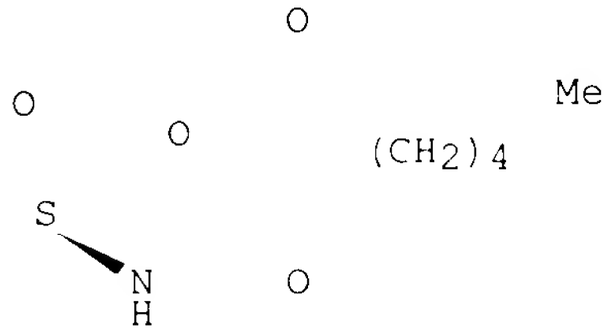
Calgary, Calgary, AB, T2N 1N4, Can.
SOURCE: Infection and Immunity (2002), 70(4), 1783-1790
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Individuals with cystic fibrosis (CF) are commonly colonized with Pseudomonas **aeruginosa**. The chronic infections caused by P. **aeruginosa** are punctuated by acute exacerbations of the lung disease, which lead to significant morbidity and mortality. As regulators of virulence determinants, P. **aeruginosa** quorum-sensing systems may be active in the chronic lung infections assocd. with CF. We have examd. the levels of autoinducer mols. and transcript accumulation from the bacterial populations found in the lungs of patients with CF. We detected biol. active levels of N-(3-oxododecanoyl)-L-homoserine (3-oxo-C12-HSL) and N-butyryl-L-homoserine lactone (C4-HSL) in sputum from CF patients. Interestingly, it appears that C4-HSL is less frequently detected than 3-oxo-C12-HSL in the lungs of patients with CF. We also examd. the transcription of the autoinducer synthase gene lasI and showed that it is frequently expressed in the lungs of patients with CF. We obsd. a significant correlation between the expression of lasI and four target genes of the Las quorum-sensing system. Taken together, our results indicate that quorum-sensing systems are active and may control virulence factor expression in the lungs of patients with CF.

IT **147795-39-9**, N-(3-Oxooctanoyl)-L-homoserine lactone
147795-40-2, N-(3-Oxodecanoyl)-L-homoserine lactone
168982-69-2, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Pseudomonas **aeruginosa** lasR-lasI quorum-sensing systems may control virulence factor expression in lungs of patients with cystic fibrosis)

RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 147795-40-2 HCAPLUS
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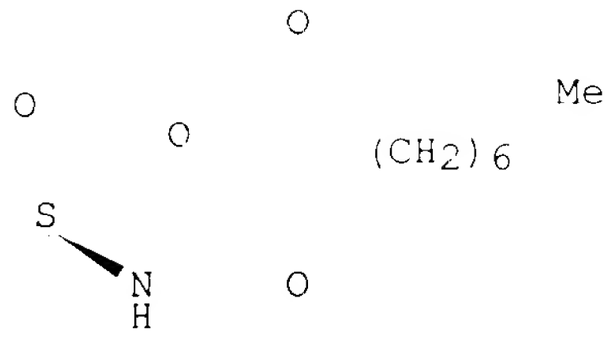
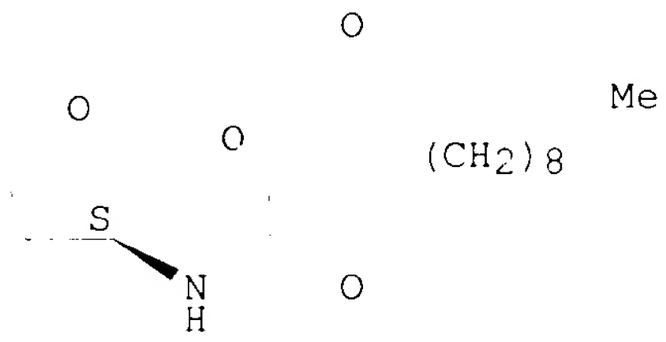
Absolute stereochemistry.



RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:171153 HCAPLUS
DOCUMENT NUMBER: 136:383992
TITLE: Direct detection of N-acylhomoserine lactones in cystic fibrosis sputum
AUTHOR(S): Middleton, Barry; Rodgers, Helen C.; Camara, Miguel; Knox, Alan J.; Williams, Paul; Hardman, Andrea
CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK
SOURCE: FEMS Microbiology Letters (2002), 207(1), 1-7
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pseudomonas **aeruginosa** and Burkholderia cepacia cause destructive lung disease in cystic fibrosis (CF) patients. Both pathogens employ 'quorum sensing', i.e. cell-to-cell communication, via diffusible N-acyl-L-homoserine lactone (AHL) signal mols., to regulate the prodn. of a no. of virulence determinants in vitro. However, to date, evidence that quorum sensing systems are functional and play a role in vivo is lacking. This study presents the first direct evidence for the presence of AHLs in CF sputum. A total of 42 samples from 25 CF patients were analyzed using lux-based Escherichia coli AHL biosensors. AHLs were detected in sputum from patients colonized by P. **aeruginosa** or B. cepacia but not Staphylococcus aureus. Furthermore, using liq.

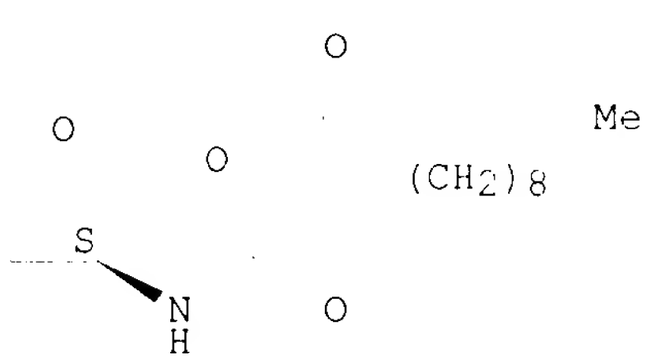
chromatog.-mass spectrometry and thin layer chromatog., we confirmed the presence of N-hexanoylhomoserine lactone and N-(3-oxododecanoyl)homoserine lactone, resp., in sputum samples from patients colonized by P. **aeruginosa**.

IT **168982-69-2**, N-(3-Oxododecanoyl)homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(direct detection of N-acylhomoserine lactones in cystic fibrosis sputum colonized by Pseudomonas **aeruginosa** and Burkholderia cepacia)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:135509 HCAPLUS
DOCUMENT NUMBER: 137:199307
TITLE: Detection of Pseudomonas **aeruginosa** cell-to-cell signals in lung tissue of cystic fibrosis patients
AUTHOR(S): Favre-Bonte, Sabine; Pache, Jean-Claude; Robert, John; Blanc, Dominique; Pechere, Jean-Claude; van Delden, Christian
CORPORATE SOURCE: Department of Genetics and Microbiology, University Hospital Geneva, Geneva, CH-1211, Switz.
SOURCE: Microbial Pathogenesis (2002), 32(3), 143-147
CODEN: MIPAEV; ISSN: 0882-4010
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chronic Pseudomonas **aeruginosa** infections lead to progressive lung tissue destruction in cystic fibrosis (CF) patients. Two bacterial cell-to-cell signals, 3-oxo-C12-HSL and C4-HSL are required for the prodn. of several extracellular virulence factors. 3-Oxo-C12-HSL is also required for the development of a differentiated biofilm, induces IL-8 prodn. by epithelial cells and possesses immunomodulatory activities. These two signaling mols. are therefore believed to play a role in the pathogenesis of P. **aeruginosa** infections, but have never been isolated from infected human tissues. We extd. and quantified the two P. **aeruginosa** cell-to-cell signals from lung tissues of two CF patients infected by P. **aeruginosa**.

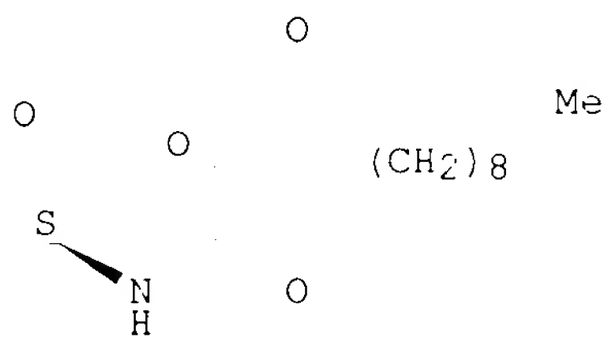
3-Oxo-C12-HSL and C4-HSL were detected in the lung tissues in fmol/g, resp. pmol/g concns.; the ratio C4-HSL/3-oxo-C12-HSL exceeded 100 in all tissue samples. Random Amplified Polymorphism DNA genotyping revealed that one genotype was present per lung. In vitro the P. **aeruginosa** isolates from the two lungs produced 3-oxo-C12-HSL, whereas some isolates did not produce detectable C4-HSL. Our results suggest that both P. **aeruginosa** cell-to-cell signals were produced in the lung tissue of these two cystic fibrosis patients.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(detection of Pseudomonas **aeruginosa** cell-to-cell signals in lung tissue of cystic fibrosis patients)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 47 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:103105 HCAPLUS

DOCUMENT NUMBER: 136:292633

TITLE: The Pseudomonas **aeruginosa** quorum-sensing molecule N-(3-oxododecanoyl)homoserine lactone contributes to virulence and induces inflammation in vivo

AUTHOR(S): Smith, Roger S.; Harris, Sarah G.; Phipps, Richard; Iglewski, Barbara

CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, Rochester, NY, 14642, USA

SOURCE: Journal of Bacteriology (2002), 184(4), 1132-1139
CODEN: JOBAAY; ISSN: 0021-9193

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pseudomonas **aeruginosa** has two well-characterized quorum-sensing systems, Las and Rhl. These systems are composed of LuxR-type proteins, LasR and RhlR, and two acyl homoserine lactone (AHL) synthases, LasI and RhlI. LasI catalyzes the synthesis of N-(3-oxododecanoyl)homoserine lactone (3O-C12-HSL), whereas RhlI catalyzes the synthesis of N-butyryl-homoserine lactone. There is little known about the importance of AHLs in vivo and what effects

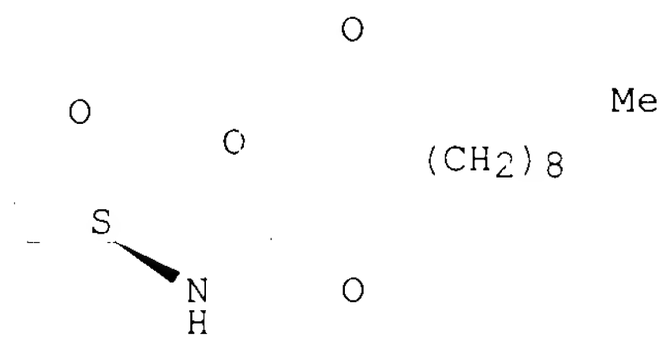
these mols. have on eukaryotic cells. In order to understand the role of AHLs in vivo, we first tested the effects that deletions of the synthase genes in P. **aeruginosa** had on colonization of the lung. We demonstrate that in an adult mouse acute-pneumonia model, deletion of the lasI gene or both the lasI and rhlI genes greatly diminished the ability of P. **aeruginosa** to colonize the lung. To det. whether AHLs have a direct effect on the host, we examd. the effects of 3O-C12-HSL injected into the skin of mice. In this model, 3O-C12-HSL stimulated a significant induction of mRNAs for the cytokines interleukin-1.alpha. (IL-1.alpha.) and IL-6 and the chemokines macrophage inflammatory protein 2 (MIP-2), monocyte chemotactic protein 1, MIP-1.beta., inducible protein 10, and T-cell activation gene 3. Addnl., dermal injections of 3O-C12-HSL also induced cyclooxygenase 2 (Cox-2) expression. The Cox-2 enzyme is important for the conversion of arachidonic acid to prostaglandins and is assocd. with edema, inflammatory infiltrate, fever, and pain. We also demonstrate that 3O-C12-HSL activates T cells to produce the inflammatory cytokine gamma interferon and therefore potentially promotes a Th1 environment. Induction of these inflammatory mediators in vivo is potentially responsible for the significant influx of white blood cells and subsequent tissue destruction assocd. with 3O-C12-HSL dermal injections. Therefore, the quorum-sensing systems of P. **aeruginosa** contribute to its pathogenesis both by regulating expression of virulence factors (exoenzymes and toxins) and by inducing inflammation.

IT **168982-69-2**, N-(3-Oxododecanoyl)homoserine lactone
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(Pseudomonas **aeruginosa** quorum-sensing mol. N-(3-oxododecanoyl)homoserine lactone contributes to virulence and induces lung and skin inflammation)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:939527 HCAPLUS
DOCUMENT NUMBER: 136:74255
TITLE: Methods for eliminating the formation of biofilm
INVENTOR(S): Xu, Feng
PATENT ASSIGNEE(S): Novozymes Biotech, Inc., USA
SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098214	A1	20011227	WO 2001-US19646	20010619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

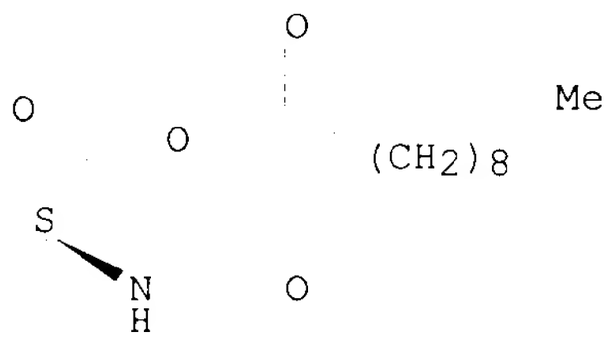
PRIORITY APPLN. INFO.: US 2000-596795 A 20000619

AB The present invention relates to methods for preventing or removing biofilm on a surface, comprising contacting the surface with an effective amt. of a compn. comprising one or more acylases and a carrier to degrade a lactone produced by one or more microorganisms, wherein the degrdn. of the lactone prevents or removes the biofilm.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: PEP (Physical, engineering or chemical process); REM (Removal or disposal); PROC (Process)
(methods for eliminating formation of biofilms using acylase compns.)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

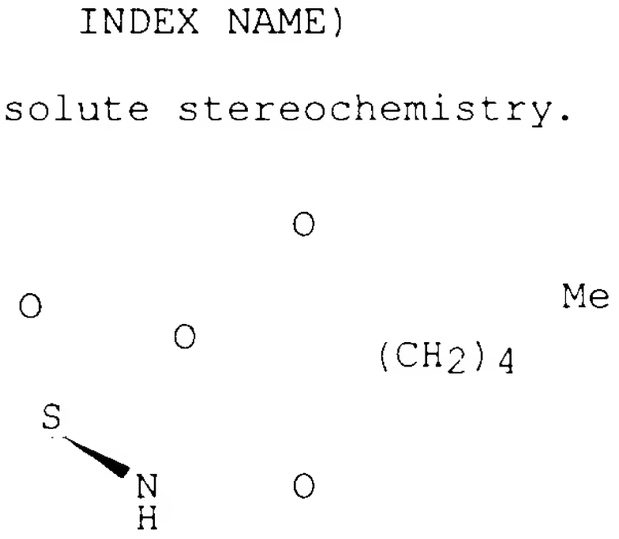
L23 ANSWER 11 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:933695 HCAPLUS
DOCUMENT NUMBER: 136:196929
TITLE: N-acylhomoserine-lactone-mediated communication between Pseudomonas **aeruginosa** and Burkholderia cepacia in mixed biofilms
AUTHOR(S): Riedel, Kathrin; Hentzer, Morten; Geisenberger,

Otto; Huber, Birgit; Steidle, Anette; Wu, Hong; Hoiby, Niels; Givskov, Michael; Molin, Soren; Eberl, Leo
CORPORATE SOURCE: Department of Microbiology, TUM, Freising, D-85350, Germany
SOURCE: Microbiology (Reading, United Kingdom) (2001), 147(12), 3249-3262
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB P. **aeruginosa** and B. cepacia are capable of forming mixed biofilms in the lungs of cystic fibrosis patients. Both bacteria employ quorum-sensing systems, which rely on N-acylhomoserine lactone (I) signal mols., to coordinate expression of virulence factors with the formation of biofilms. As both bacteria utilize the same class of signal mols., the authors investigated whether communication between the species occurs. To address this issue, novel Gfp-based biosensors for non-destructive, in situ detection of Is were constructed and characterized. These sensors were used to visualize I-mediated communication in mixed biofilms, which were cultivated either in artificial flow chambers or in alginate beads in mouse lung tissue. In both model systems, B. cepacia was capable of perceiving the I signals produced by P. **aeruginosa**, while the latter strain did not respond to the mols. produced by B. cepacia. Measurements of extracellular proteolytic activities of defined quorum-sensing mutants grown in media complemented with I exts. prepd. from culture supernatants of various wild-type and mutant strains supported the view of unidirectional signalling between the 2 strains.

IT **147795-39-9**, Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- **168982-69-2**, Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- **177158-19-9**, Tetradecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]-
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(N-acylhomoserine-lactone-mediated communication between Pseudomonas **aeruginosa** and Burkholderia cepacia in mixed biofilms)

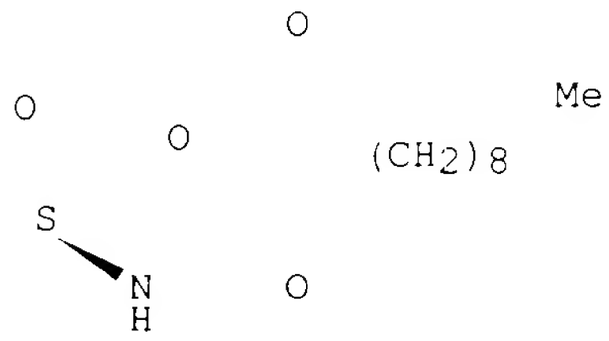
RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



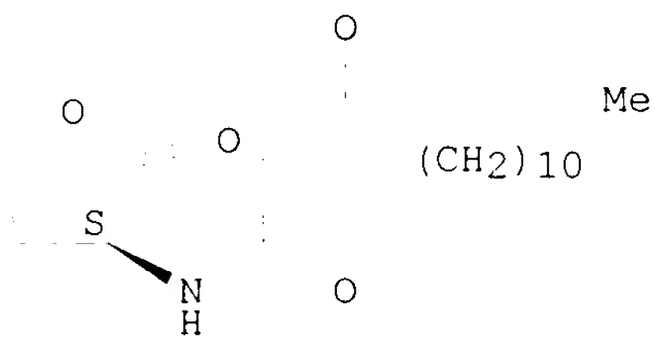
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177158-19-9 HCAPLUS
CN Tetradecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

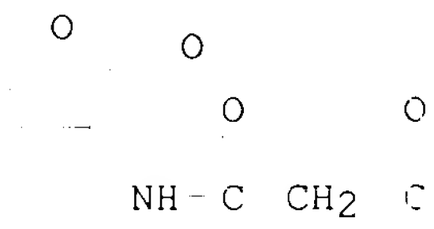
L23 ANSWER 12 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:914725 HCAPLUS
DOCUMENT NUMBER: 136:364772
TITLE: A quorum sensing-associated virulence gene of Pseudomonas **aeruginosa** encodes a LysR-like transcription regulator with a unique self-regulatory mechanism
AUTHOR(S): Cao, Hui; Krishnan, Gomathi; Goumnerov, Boyan; Tsongalis, John; Tompkins, Ronald; Rahme, Laurence G.
CORPORATE SOURCE: Department of Surgery, Harvard Medical School, Massachusetts General Hopital and Boston Shriners Institute, Boston, MA, 02114, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(25), 14613-14618
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human opportunistic pathogen Pseudomonas **aeruginosa** strain PA14 infects both plants and animals. Previously, using plants to screen directly for P. **aeruginosa** virulence-attenuated mutants, we identified a locus, pho34B12, relevant in mammalian pathogenesis. Here, nonsense point mutations

in the two opposing ORFs identified in the pho34B12 locus revealed that one of them, mvfR (multiple virulence factor Regulator), is able to control all of the phenotypes that mutant phoA34B12 displays. Both genetic and biochem. evidence demonstrate that the mvfR gene encodes a LysR-like transcriptional factor that pos. regulates the prodn. of elastase, phospholipase, and of the autoinducers, 3-oxo-dodecanoyl homoserine lactone (PAI 1) and 2-heptyl-3-hydroxy-4-quinolone (PQS), as well as the expression of the phnAB operon, involved in phenazine biosynthesis. We demonstrate that the MvfR protein is membrane-assocd. and acts as a transcriptional activator until cells reach stationary phase, when a unique neg. feedback mechanism is activated to signal the downregulation of the MvfR protein. This work reveals an unprecedented virulence mechanism of P. **aeruginosa** and identifies a unique indispensable player in the P. **aeruginosa** quorum-sensing cascade.

IT **152833-54-0**, -Dodecanamide 3-Oxo-N-(tetrahydro-2-oxo-3-furanyl)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PAI-1 (P. **aeruginosa** autoinducer), MvfR controls prodn. of; quorum sensing-assocd. virulence gene of Pseudomonas **aeruginosa** encodes LysR-like transcription regulator with unique self-regulatory mechanism)

RN 152833-54-0 HCAPLUS

CN Dodecanamide, 3-oxo-N-(tetrahydro-2-oxo-3-furanyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 13 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:811536 HCAPLUS
DOCUMENT NUMBER: 136:306525
TITLE: The global posttranscriptional regulator RsmA modulates production of virulence determinants and N-acylhomoserine lactones in Pseudomonas **aeruginosa**
AUTHOR(S): Pessi, Gabriella; Williams, Faye; Hindle, Zoe; Heurlier, Karin; Holden, Matthew T. G.; Camara, Miguel; Haas, Dieter; Williams, Paul
CORPORATE SOURCE: Laboratoire de Biologie Microbienne, Universite de Lausanne, Lausanne, CH-1015, Switz.
SOURCE: Journal of Bacteriology (2001), 183(22), 6676-6683
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Posttranscriptional control is known to contribute to the regulation

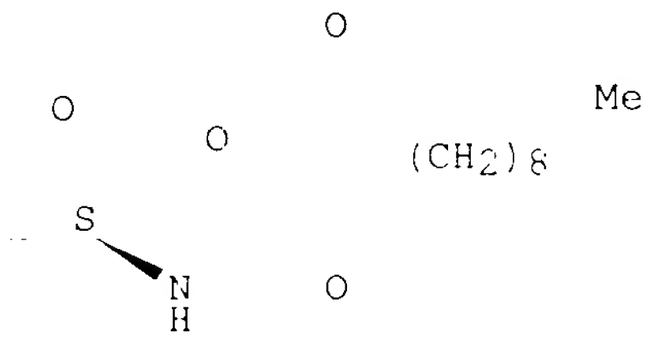
of secondary metab. and virulence determinants in certain gram-neg. bacteria. A Pseudomonas **aeruginosa** gene was isolated which encodes a global translational regulatory protein, RsmA (regulator of secondary metabolites). Overexpression of rsmA resulted in a substantial redn. in the levels of extracellular products, including protease, elastase, and staphylolytic (LasA protease) activity as well as the PA-IL lectin, hydrogen cyanide (HCN), and the phenazine pigment pyocyanin. While inactivation of rsmA in P. **aeruginosa** had only minor effects on the extracellular enzymes and the PA-IL lectin, the prodn. of HCN and pyocyanin was enhanced during the exponential phase. The influence of RsmA on N-acylhomoserine lactone-mediated quorum sensing was detd. by assaying the levels of N-(3-oxododecanoyl)homoserine lactone (3-oxo-C12-HSL) and N-butanoylhomoserine lactone (C4-HSL) produced by the rsmA mutant and the rsmA-overexpressing strain. RsmA exerted a neg. effect on the synthesis of both 3-oxo-C12-HSL and C4-HSL, which was confirmed by using lasI and rhlI translational fusions. These data also highlighted the temporal expression control of the lasI gene, which was induced much earlier and to a higher level during the exponential growth phase in an rsmA mutant. To investigate whether RsmA modulates HCN prodn. solely via quorum-sensing control, hcn translational fusions were employed to monitor the regulation of the cyanide biosynthesis genes (hcnABC). RsmA was shown to exert an addnl. neg. effect on cyanogenesis posttranscriptionally by acting on a region surrounding the hcnA ribosome-binding site. This suggests that, in P. **aeruginosa** , RsmA functions as a pleiotropic posttranscriptional regulator of secondary metabolites directly and also indirectly by modulating the quorum-sensing circuitry.

IT **168982-69-2**, N-(3-Oxododecanoyl)homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(global posttranscriptional regulator RsmA modulates prodn. of virulence determinants and N-acylhomoserine lactones in Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:658967 HCAPLUS
DOCUMENT NUMBER: 136:50797
TITLE: Stringent response activates quorum sensing and

modulates cell density-dependent gene expression in Pseudomonas **aeruginosa**

AUTHOR(S): Van Delden, Christian; Comte, Rachel; Bally, Marc

CORPORATE SOURCE: Department of Genetics and Microbiology, University of Geneva Medical School, Geneva, CH-1211/4, Switz.

SOURCE: Journal of Bacteriology (2001), 183(18), 5376-5384
CODEN: JOBAAY; ISSN: 0021-9193

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

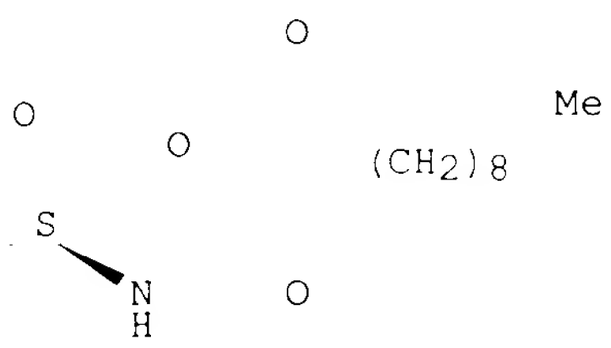
AB During nutrient starvation, Escherichia coli elicits a stringent response involving the ribosome-assocd. protein RelA. Activation of RelA results in a global change in the cellular metab. including enhanced expression of the stationary-phase sigma factor RpoS. In the human pathogen P. **aeruginosa**, a complex quorum-sensing circuitry, linked to RpoS expression, is required for cell d.-dependent prodn. of many secreted virulence factors, including LasB elastase. Quorum sensing relies on the activation of specific transcriptional regulators (LasR and RhlR) by their corresponding autoinducers (3-oxo-C12-homoserine lactone [HSL] and C4-HSL), which function as intercellular signals. Overexpression of relA activates the expression of rpoS in P. **aeruginosa** and leads to premature, cell d.-independent LasB elastase prodn. Therefore, the effects of the stringent response on quorum sensing were investigated. Both lasR and rhlR gene expression and autoinducer synthesis were prematurely activated during the stringent response induced by overexpression of relA. Premature expression of lasR and rhlR was also obsd. when relA was overexpressed in a PAO1 rpoS mutant. The stringent response induced by the amino acid analog serine hydroxamate (SHX) also led to premature prodn. of the 3-oxo-C12-HSL autoinducer. This response to SHX was absent in a PAO1 relA mutant. These findings suggest that the stringent response can activate the 2 quorum-sensing systems of P. **aeruginosa** independently of cell d.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study) (stringent response activates quorum sensing and modulates cell d.-dependent gene expression in Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE

Searcher : Shears 308-4994

FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:612412 HCAPLUS
DOCUMENT NUMBER: 136:35639
TITLE: Haemodynamic effects of the bacterial quorum sensing signal molecule, N-(3-oxododecanoyl)-L-homoserine lactone, in conscious, normal and endotoxaemic rats
AUTHOR(S): Gardiner, S. M.; Chhabra, S. R.; Harty, C.; Williams, P.; Pritchard, D. I.; Bycroft, B. W.; Bennett, T.
CORPORATE SOURCE: School of Biomedical Sciences, - Queen's Medical Centre, University of Nottingham, Nottingham, NG7 2UH, UK
SOURCE: British Journal of Pharmacology (2001), 133(7), 1047-1054
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-acylhomoserine lactones (AHLs) are small, diffusible signaling mols., employed by Gram-neg. bacteria to coordinate gene expression with cell population d. Recent in vitro findings indicate that AHLs may function as virulence determinants per se, through modification of cytokine prodn. by eukaryotic cells, and by stimulating the relaxation of blood vessels. In the present study, we assessed the influence of AHLs on cardiovascular function in conscious rats, and draw attention to the ability of the N-(3-oxododecanoyl)-L-homoserine lactone (3-oxo-C12-HSL), a signal mol. produced by P. **aeruginosa**, to cause marked bradycardia. This bradycardic effect was blocked by atropine and atenolol, and did not occur in vitro. Furthermore, modification of the acyl side chain length resulted in the loss of activity, whereas removal of the homoserine lactone ring, did not. The bradycardic effect of 3-oxo-C12-HSL was also obsd. in endotoxemic animals, albeit attenuated. In normal rats, 3-oxo-C12-HSL caused initial mesenteric and hindquarters vasoconstriction, but only slight, and delayed signs of vasodilatation in the renal and mesenteric vascular beds. Furthermore, administration of 3-oxo-C12-HSL (pre-treatment or 2 h post-treatment) together with LPS, did not modify the established regional hemodynamic effects of the LPS, 6 h after the onset of its infusion. Our observations do not provide any clear evidence for an ability of 3-oxo-C12-HSL to modify the hemodynamic responses to LPS infusion. However, they are not inconsistent with the hypothesis that some of the cardiovascular sequelae of bacterial infection may be modulated by an influence of bacterial quorum sensing signaling mols. on the host.

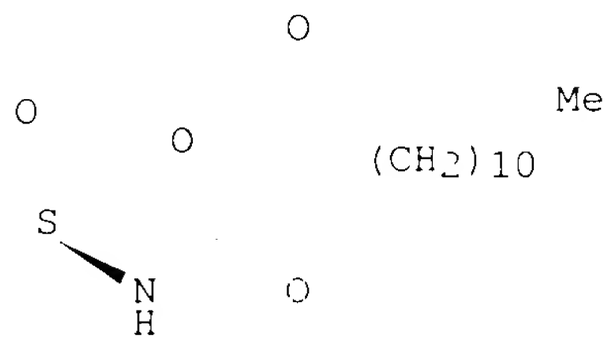
IT **177158-19-9**, N-(3-Oxotetradecanoyl)-L-homoserine lactone
216596-70-2 216596-73-5 364749-87-1
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(comparison; hemodynamic effects of the bacterial quorum sensing signal mol., N-(3-oxododecanoyl)-L-homoserine lactone, in conscious, normal and endotoxemic rats)

RN 177158-19-9 HCAPLUS

Searcher : Shears 308-4994

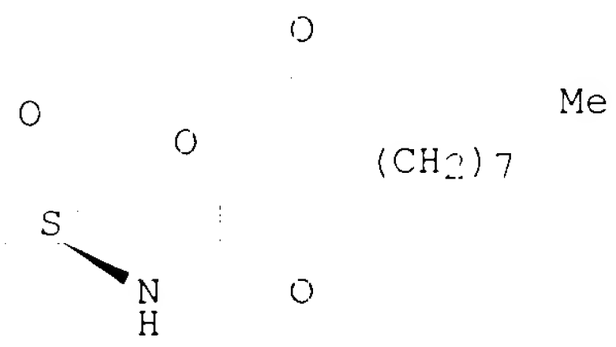
CN Tetradecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



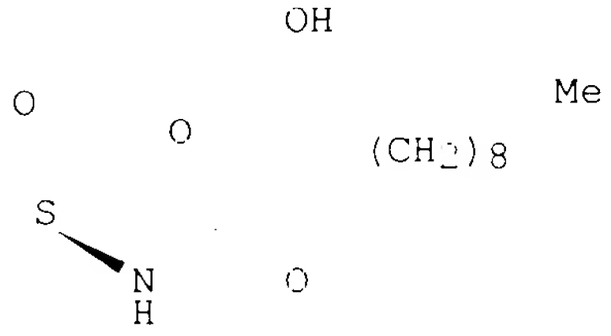
RN 216596-70-2 HCAPLUS
CN Undecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



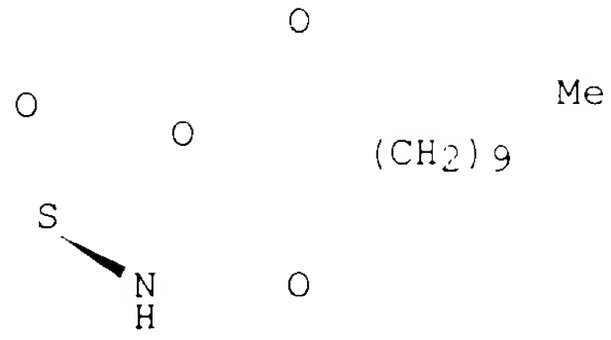
RN 216596-73-5 HCAPLUS
CN Dodecanamide, 3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



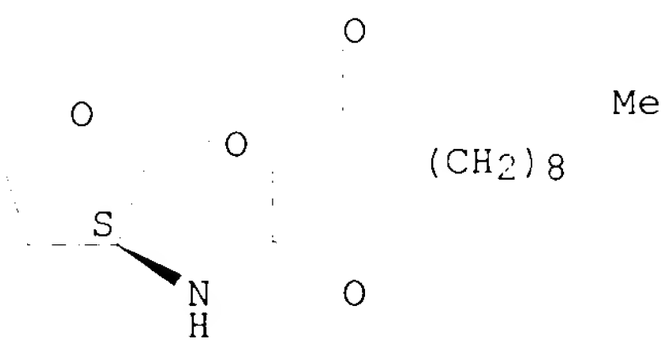
RN 364749-87-1 HCAPLUS
CN Tridecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(hemodynamic effects of the bacterial quorum sensing signal mol., N-(3-oxododecanoyl)-L-homoserine lactone, in conscious, normal and endotoxemic rats)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 16 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:490495 HCAPLUS
DOCUMENT NUMBER: 135:239130
TITLE: Reaction of acylated homoserine lactone bacterial signaling molecules with oxidized halogen antimicrobials
AUTHOR(S): Borchardt, S. A.; Allain, E. J.; Michels, J. J.; Stearns, G. W.; Kelly, R. F.; McCoy, W. F.
CORPORATE SOURCE: Global Research, ONDEO Nalco, Naperville, IL, 60563, USA
SOURCE: Applied and Environmental Microbiology (2001), 67(7), 3174-3179
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Oxidized halogen antimicrobials, such as hypochlorous and hypobromous acids, have been used extensively for microbial control in industrial systems. Recent discoveries have shown that acylated homoserine lactone cell-to-cell signaling mols. are important for

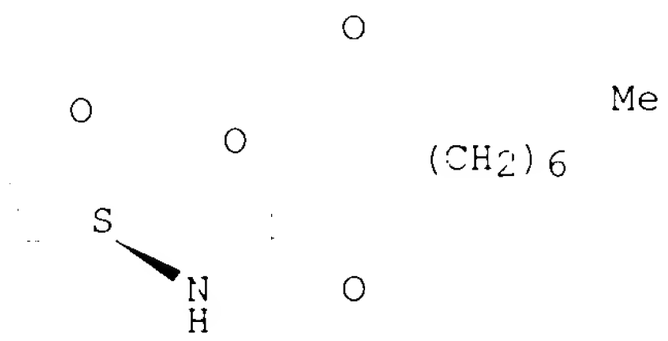
biofilm formation in Pseudomonas **aeruginosa**, suggesting that biofouling can be controlled by interfering with bacterial cell-to-cell communication. This study was conducted to investigate the potential for oxidized halogens to react with acylated homoserine lactone-based signaling mols. Acylated homoserine lactones contg. a 3-oxo group were found to rapidly react with oxidized halogens, while acylated homoserine lactones lacking the 3-oxo functionality did not react. The Chromobacterium violaceum CV026 bioassay was used to det. the effects of such reactions on acylated homoserine lactone activity. The results demonstrated that 3-oxo acyl homoserine lactone activity was rapidly lost upon exposure to oxidized halogens; however, acylated homoserine lactones lacking the 3-oxo group retained activity. Expts. with the marine alga Laminaria digitata demonstrated that natural haloperoxidase systems are capable of mediating the deactivation of acylated homoserine lactones. This may illustrate a natural defense mechanism to prevent biofouling on the surface of this marine alga. The Chromobacterium violaceum activity assay illustrates that reactions between 3-oxo acylated homoserine lactone mols. and oxidized halogens do occur despite the presence of biofilm components at much greater concns. This work suggests that oxidized halogens may control biofilm not only via a cidal mechanism, but also by possibly interfering with 3-oxo acylated homoserine lactone-based cell signaling.

IT **147795-40-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of acylated homoserine lactone bacterial signaling mols. with oxidized halogen antimicrobials in relation to biofilm and biofouling control)

RN 147795-40-2 HCAPLUS

CN Decanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 17 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:471002 HCAPLUS
DOCUMENT NUMBER: 135:209777
TITLE: IL-8 production in human lung fibroblasts and epithelial cells activated by the Pseudomonas autoinducer N-3-oxododecanoyl homoserine lactone is transcriptionally regulated by NF-.kappa.B and activator protein-2
AUTHOR(S): Smith, Roger S.; Fedyk, Eric R.; Springer, T.

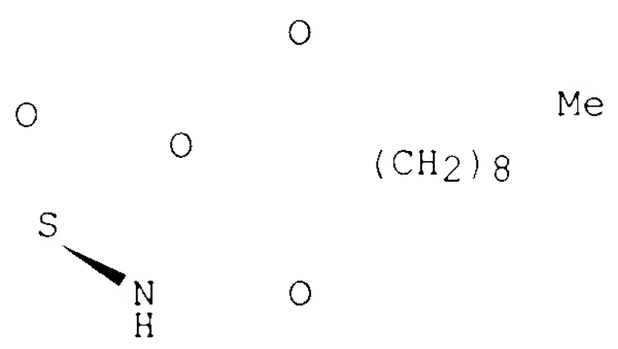
Searcher : Shears 308-4994

A.; Mukaida, N.; Iglewski, Barbara H.; Phipps, Richard P.
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, Rochester, NY, 14642, USA
SOURCE: Journal of Immunology (2001), 167(1), 366-374
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The destructive pulmonary inflammation assocd. with Pseudomonas **aeruginosa** colonization is caused, in part, by the prodn. of the chemokine IL-8, which recruits neutrophils into the lung. The Pseudomonas autoinducer, N-3-oxododecanoyl homoserine lactone (3-O-C12-HSL), is a small lipid-sol. mol. that is essential in the regulation of many P. **aeruginosa** virulence factors, but little is known about how it affects eukaryotic cells. Here, the authors demonstrate that 3-O-C12-HSL is a potent stimulator of both IL-8 mRNA and protein from human fibroblasts and epithelial cells in vitro. The IL-8 produced from these 3-O-C12-HSL-stimulated cells was functionally active by inducing the chemotaxis of neutrophils. To det. a mechanism for this IL-8 induction, deletion constructs of the IL-8 promoter were examd. It was found that the DNA region between nucleotides -1481 and -546 and the transcription factor NF-.kappa.B were essential for the maximal induction of IL-8 by 3-O-C12-HSL. This was confirmed by EMSAs, where 3-O-C12-HSL induced a shift with both AP-2 and NF-.kappa.B consensus DNA. The activation of NF-.kappa.B and subsequent prodn. of IL-8 were regulated by a mitogen-activated protein kinase pathway. Thus, the severe lung damage that accompanies P. **aeruginosa** infections is caused by an exuberant neutrophil response stimulated by 3-O-C12-HSL-induced IL-8. Understanding the mechanisms of 3-O-C12-HSL activation of lung structural cells may provide a means to help control lung damage during infections with P. **aeruginosa.**

IT **168982-69-2**, N-3-Oxododecanoyl homoserine lactone
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(interleukin-8 formation in human lung fibroblasts and epithelial cells activated by Pseudomonas autoinducer (N-3-oxododecanoyl homoserine lactone) is transcriptionally regulated by NF-.kappa.B and activator protein-2)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

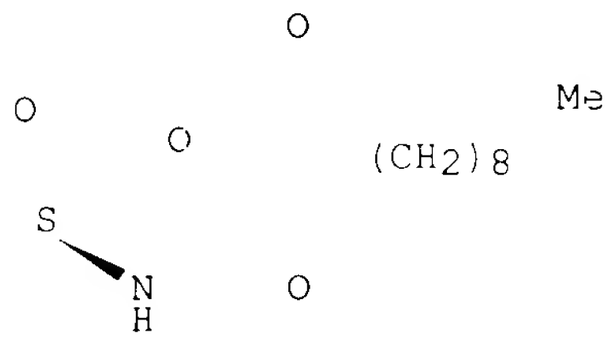


Searcher : Shears 308-4994

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 18 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:378988 HCAPLUS
DOCUMENT NUMBER: 135:119485
TITLE: Azithromycin inhibits quorum sensing in Pseudomonas **aeruginosa**
AUTHOR(S): Tateda, Kazuhiro; Comte, Rachel; Pechere, Jean-Claude; Kohler, Thilo; Yamaguchi, Keizo; Van Delden, Christian
CORPORATE SOURCE: Department of Microbiology, Toho University School of Medicine, Tokyo, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2001), 45(6), 1930-1933
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two .mu.g of azithromycin/mL inhibited the quorum-sensing circuitry of P. **aeruginosa** strain PAO1. Addn. of synthetic autoinducers partially restored the expression of the transcriptional activator-encoding genes lasR and rhlR but not that of the autoinducer synthase-encoding gene lasI. Azithromycin apparently interferes with the synthesis of autoinducers by an unknown mechanism, leading to a redn. of virulence factor prodn.
IT **168982-69-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(azithromycin inhibits quorum sensing in Pseudomonas **aeruginosa**)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 19 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:176554 HCAPLUS
DOCUMENT NUMBER: 135:283360
TITLE: QscR, a modulator of quorum-sensing signal synthesis and virulence in Pseudomonas **aeruginosa**

Searcher : Shears 308-4994

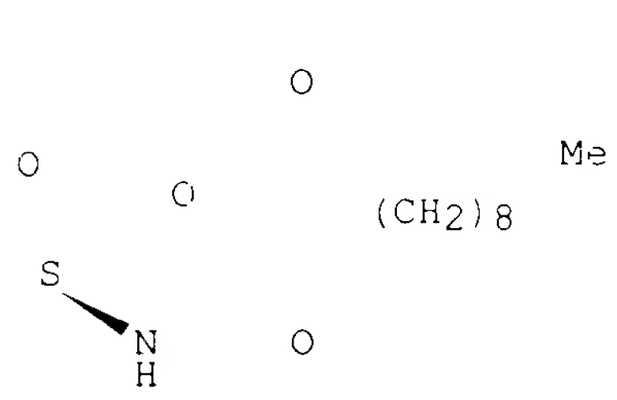
AUTHOR(S): Chugani, Sudha A.; Whiteley, Marvin; Lee, Kimberly M.; D'Argenio, David; Manoil, Colin; Greenberg, E. P.
CORPORATE SOURCE: Department of Microbiology, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(5), 2752-2757
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The opportunistic pathogenic bacterium Pseudomonas **aeruginosa** uses quorum-sensing signaling systems as global regulators of virulence genes. There are two quorum-sensing signal receptor and signal generator pairs, LasR-LasI and RhlR-RhlI. The recently completed P. **aeruginosa** genome-sequencing project revealed a gene coding for a homolog of the signal receptors, LasR and RhlR. Here the authors describe a role for this gene, which the authors call qscR. The qscR gene product governs the timing of quorum-sensing-controlled gene expression and it dampens virulence in an insect model. The authors present evidence that suggests the primary role of QscR is repression of lasI. A qscR mutant produces the LasI-generated signal prematurely, and this results in premature transcription of a no. of quorum-sensing-regulated genes. When fed to Drosophila melanogaster, the qscR mutant kills the animals more rapidly than the parental P. **aeruginosa**. The repression of lasI by QscR could serve to ensure that quorum-sensing-controlled genes are not activated in environments where they are not useful.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(qscR gene encodes a modulator of quorum-sensing signal synthesis and virulence in Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 20 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:60934 HCAPLUS
DOCUMENT NUMBER: 134:277828

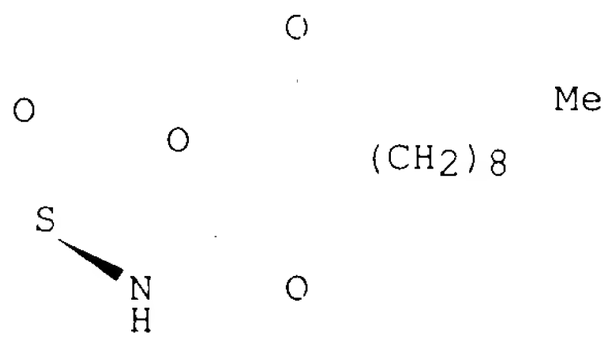
TITLE: A mathematical model for quorum sensing in Pseudomonas **aeruginosa**
AUTHOR(S): Dockery, Jack D.; Keener, James P.
CORPORATE SOURCE: Department of Mathematics, Montana State University, Bozeman, MT, 59718, USA
SOURCE: Bulletin of Mathematical Biology (2001), 63(1), 95-116
CODEN: BMTBAP; ISSN: 0092-8240
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bacteria Pseudomonas **aeruginosa** use the size and d. of their colonies to regulate the prodn. of a large variety of substances, including toxins. This phenomenon, called quorum sensing, apparently enables colonies to grow to sufficient size undetected by the immune system of the host organism. In this paper, we present a math. model of quorum sensing in P. **aeruginosa** that is based on the known biochem. of regulation of the autoinducer that is crucial to this signalling mechanism. Using this model we show that quorum sensing works because of a biochem. switch between two stable steady solns., one with low levels of autoinducer and one with high levels of autoinducer. (c) 2001 Society for Mathematical Biology.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserinelactone
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(autoinducer; math. model for quorum sensing in Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 21 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:875579 HCAPLUS
DOCUMENT NUMBER: 134:249050
TITLE: A novel and sensitive method for the quantification of N-3-oxoacyl homoserine lactones using gas chromatography-mass spectrometry: application to a model bacterial biofilm

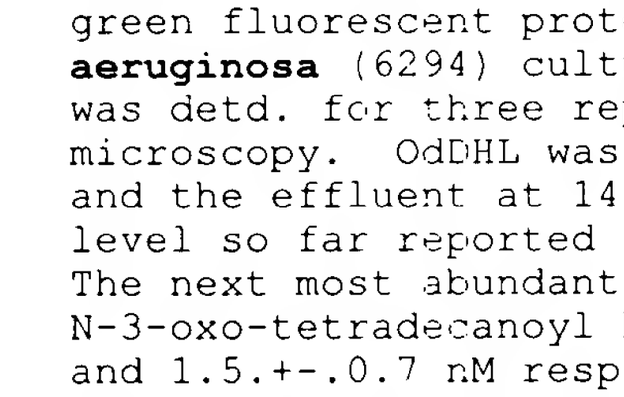
Searcher : Shears 308-4994

AUTHOR(S): Charlton, Timothy S.; De Nys, Rocky; Netting, Andrew; Kumar, Naresh; Hentzer, Morten; Givskov, Michael; Kjelleberg, Staffan
CORPORATE SOURCE: School of Microbiology and Immunology, University of New South Wales, 2052, Australia
SOURCE: Environmental Microbiology (2000), 2(5), 530-541
CODEN: ENMIFM; ISSN: 1462-2912
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method is reported for the quantification of 3-oxoacyl homoserine lactones (3-oxo AHLs), a major class of quorum-sensing signals found in Gramneg. bacteria. It is based on the conversion of 3-oxo AHLs to their pentafluorobenzyloxime derivs. followed by gas chromatog.-mass spectrometry (electron capture-neg. ion). The method used [13C16]-N-3-oxo-dodecanoyl homoserine lactone ([13C16]-OdDHL) as the internal std., and its validity was tested by spiking the supernatant and cell fractions with three levels of 3-oxo AHLs, i.e. 1, 10 and 100 ng per sample. These showed the method to be both sensitive (S/N ratio > 10:1 for 1 ng) and accurate. The assay was applied to the biofilm and effluent of a green fluorescent protein (GFP)-expressing strain of Pseudomonas **aeruginosa** (6294) culture grown in flow cells. Biofilm vol. was detd. for three replicate flow cells by confocal scanning laser microscopy. OdDHL was detected in the biofilm at 632.+-.381 .mu.M and the effluent at 14.+-.3 nM. The biofilm concn. is the highest level so far reported for an AHL in a wild-type bacterial system. The next most abundant 3-oxo AHL in the biofilm and effluent was N-3-oxo-tetradecanoyl homoserine lactone (OtDHL) at 40.+-.15 .mu.M and 1.5.+-.0.7 nM resp. OtDHL is unreported for P. **aeruginosa** and has an activity equiv. to OdDHL in a lasR bioassay. Two other 3-oxo AHLs were detected at lower concns.: N-3-oxo-decanoyl homoserine lactone (ODHL) in the biofilm (3.+-.2 .mu.M) and effluent (1.+-.0.1 nM); and N-3-oxo-octanoyl homoserine lactone (OOHL) in the effluent (0.1.+-.0.1 nM).

IT **147795-39-9 147795-40-2 168982-69-2,** N-3-Oxo-dodecanoyl homoserine lactone **177158-19-9**
RL: ANT (Analyte); ANST (Analytical study)
(N-3-oxoacyl homoserine lactones detn. using gas chromatog.-mass spectrometry)

RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

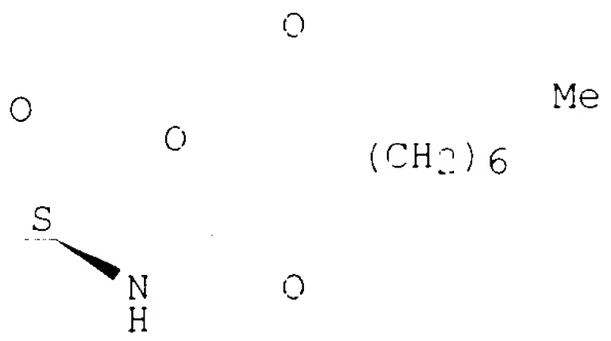
Absolute stereochemistry.



RN 147795-40-2 HCAPLUS
CN Decanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA

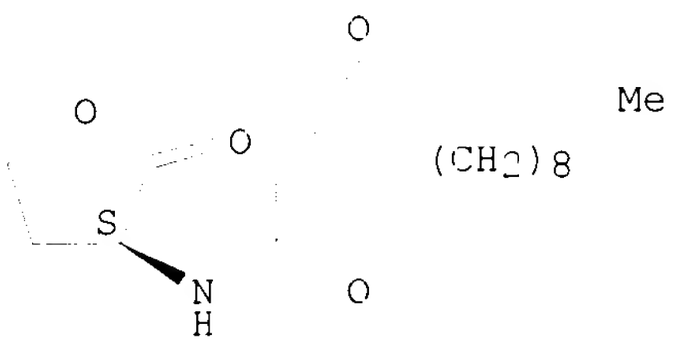
INDEX NAME)

Absolute stereochemistry.



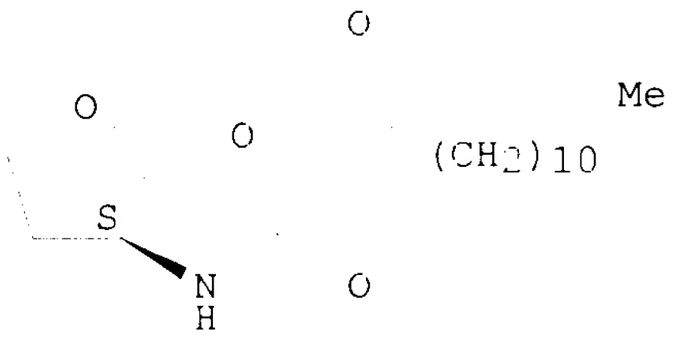
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177158-19-9 HCAPLUS
CN Tetradecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 22 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:771105 HCAPLUS
DOCUMENT NUMBER: 134:68618
TITLE: Effects of quorum sensing signal molecules on the hydrogen peroxide resistance against planktonic Pseudomonas **aeruginosa**
AUTHOR(S): Huang, Ching-Tsan; Shih, Pei-Chin
CORPORATE SOURCE: Department of Agricultural Chemistry, National

Taiwan University, Taipei, 10617, Taiwan
SOURCE: Journal of Microbiology, Immunology and Infection (2000), 33(3), 154-158
CODEN: JMIIFG
PUBLISHER: Chinese Society of Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

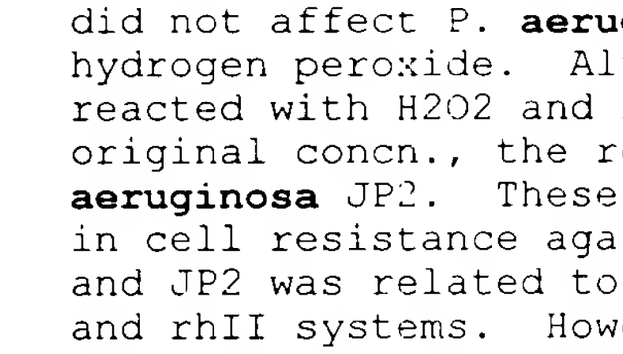
AB The effects of quorum sensing signal mols. in Pseudomonas **aeruginosa**, N-butanoyl-L-homoserinelactone (C4-HSL) and N-(3-oxododecanoyl)-L-homoserinelactone (3-oxo-C12-HSL), on planktonic cell resistance against hydrogen peroxide were studied. In P. **aeruginosa** JP2 cells with the deletion of lasI and rhII, the viable cell concn. decreased with time and was reduced by about 4 log after 2 h of 7.5 mM H2O2 treatment, while only a 2-log redn. was found for the wild type P. **aeruginosa** PAO1 cells. When cultured with 20% PAO1 spent medium, P. **aeruginosa** JP2 showed similar hydrogen peroxide resistance to that seen in P. **aeruginosa** PAO1. Culturing with 20% JP2 spent medium or with 10 .mu.M C4-HSL and 20 .mu.M 3-oxo-C12-HSL did not affect P. **aeruginosa** JP2 cell susceptibility to hydrogen peroxide. Although both 20% PAO1 and JP2 spent media reacted with H2O2 and reduced H2O2 to 50% of the strength of the original concn., the remaining H2O2 was still sufficient to kill P. **aeruginosa** JP2. These results indicate that the difference in cell resistance against H2O2 between P. **aeruginosa** PAO1 and JP2 was related to the existence of gene products of the lasI and rhII systems. However, adding synthetic homoserine lactones alone did not increase P. **aeruginosa** JP2 cell resistance to H2O2 as seen in the expts. adding PAO1 spent medium. Detn. of the detailed relation between cascade regulation in P. **aeruginosa** and its cell resistance to H2O2 will require further investigation.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserinelactone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of quorum sensing signal mols. on hydrogen peroxide resistance in Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 23 OF 47 HCAPLUS COPYRIGHT 2002 ACS

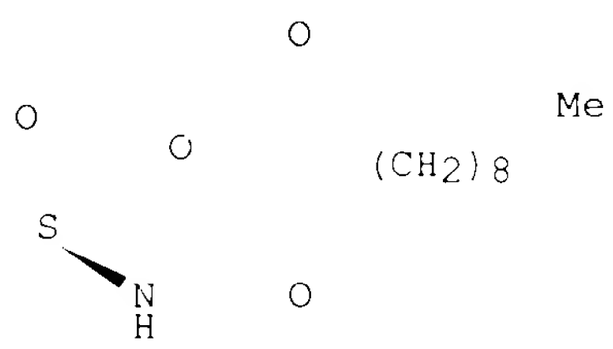
Searcher : Shears 308-4994

ACCESSION NUMBER: 2000:751815 HCAPLUS
DOCUMENT NUMBER: 134:40394
TITLE: Quorum-sensing signals indicate that cystic fibrosis lungs are infected with bacterial biofilms
AUTHOR(S): Singh, Pradeep K.; Schaefer, Amy L.; Parsek, Matthew R.; Moninger, Thomas O.; Welsh, Michael J.; Greenberg, E. P.
CORPORATE SOURCE: Howard Hughes Med. Inst., Univ. Iowa College Med., Iowa City, IA, 52242, USA
SOURCE: Nature (London) (2000), 407(6805), 762-764
CODEN: NATJAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bacterium Pseudomonas **aeruginosa** permanently colonizes cystic fibrosis lungs despite aggressive antibiotic treatment. This suggests that P. **aeruginosa** might exist as biofilms - structured communities of bacteria encased in a self-produced polymeric matrix - in the cystic fibrosis lung. Consistent with this hypothesis, microscopy of cystic fibrosis sputum shows that P. **aeruginosa** are in biofilm-like structures, P. **aeruginosa** uses extracellular quorum-sensing signals (extracellular chem. signals that cue cell-d.-dependent gene expression) to coordinate biofilm formation. Here we found that cystic fibrosis sputum produces the two principal P. **aeruginosa** quorum-sensing signals; however, the relative abundance of these signals as opposite to that of the std. P. **aeruginosa** strain PAO1 in lab. broth culture. When P. **aeruginosa** sputum isolates were grown in broth, some showed quorum-sensing signal ratios like those of the lab. strain. When we grew these isolates and PAO1 in a lab. biofilm model, the signal ratios were like those in cystic fibrosis sputum. Our data support the hypothesis that P. **aeruginosa** are in a biofilm in cystic fibrosis sputum. Moreover, quorum-sensing signal profiling of specific P. **aeruginosa** strains may serve as a biomarker in screens to identify agents that interfere with biofilm development.

IT **168982-69-2**, N-(3-Oxo-dodecanoyl)-L-homoserine lactone
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(quorum-sensing signals indicate that human cystic fibrosis lungs are infected with bacterial biofilms)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Searcher : Shears 308-4994

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 24 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:133843 HCAPLUS
DOCUMENT NUMBER: 132:176614
TITLE: Gene switch for target gene transcription using inducible promoters and response proteins
INVENTOR(S): Martinez, Alberto; Jepson, Ian; Fray, Rupert George
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009704	A1	20000224	WO 1999-GB2653	19990812
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335651	AA	20000224	CA 1999-2335651	19990812
AU 9953796	A1	20000306	AU 1999-53796	19990812
EP 1104472	A1	20010606	EP 1999-939526	19990812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002522079	T2	20020723	JP 2000-565139	19990812

PRIORITY APPLN. INFO.: GB 1998-17704 A 19980813
WO 1999-GB2653 W 19990812

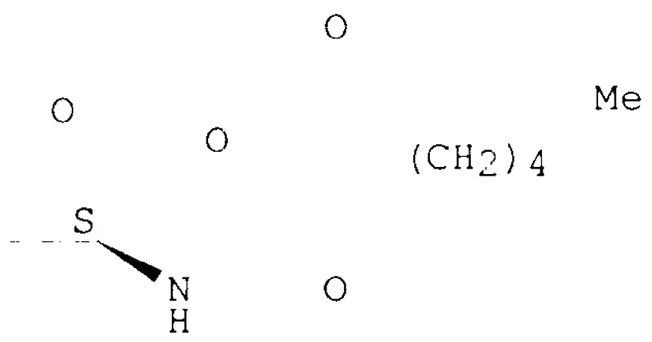
AB The present invention relates to a method of initiating transcription of a target gene in a eukaryotic cell comprising: (a) providing a eukaryotic cell which is capable of producing a response protein; and (b) inserting into the genome of said cell a polynucleotide defining an inducible promoter sequence operably linked to and capable when induced of initiating transcription of said target gene; and (c) applying to said cell a chem. inducer capable of binding to said response protein whereby said chem. inducer binds to said response protein to form an inducing complex which binds to and induces said inducible promoter thereby initiating transcription of said target gene. Three specific gene switch systems are described: (a) the TraR response regulator of Agrobacterium tumefaciens with the inducer N-(3-oxo)octanoyl-L-homoserine lactone (OOHL); (b) the LuxR response regulator of Photobacterium fischeri with either OOHL or N-(3-oxo)hexanoyl-L-homoserine lactone (OHHL) as inducer; and (3) the LasR system of Pseudomonas **aeruginosa** with N-(3-oxo)dodecanoyl-L-homoserine lactone as inducer. The luxR system is inducible by OHHL

or N-hexanoyl-L-homoserine lactone for stable expression of the yenI gene from Yersinia enterocolitica in tobacco plants. Inducible promoters may include the Alc A/R switch system, the GST switch system, and the ecdysone switch. The present invention therefore provides a gene switch whereby expression of a foreign gene(s) may be controlled by application of an effective exogenous inducer.

IT **147795-39-9**, N-(3-Oxo)-octanoyl-L-homoserine lactone
168982-69-2, N-(3-Oxo)-dodecanoyl-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(gene switch for target gene transcription using inducible promoters and response proteins)

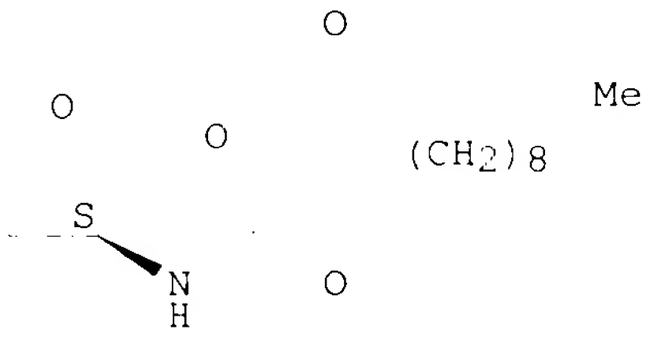
RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 25 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:112434 HCAPLUS
DOCUMENT NUMBER: 133:23216
TITLE: Extraction of violacein from Chromobacterium violaceum provides a new quantitative bioassay for N-acyl homoserine lactone autoinducers
AUTHOR(S): Blosser, R. S.; Gray, K. M.
CORPORATE SOURCE: Department of Biology, University of South Florida, Tampa, FL, USA
SOURCE: Journal of Microbiological Methods (2000),

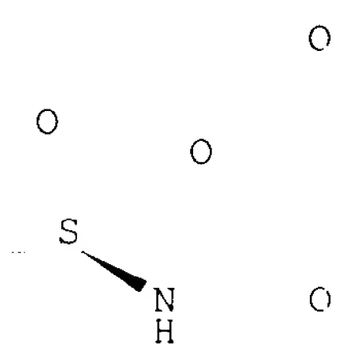
40(1), 47-55
CODEN: JMIMDQ; ISSN: 0167-7012
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fatty acyl homoserine lactones (AHLs) are used as extracellular quorum sensing signals by a variety of Gram-neg. bacteria. By activating proteins belonging to the LuxR family of transcriptional regulators, these signal metabolites allow population d.-dependent gene regulation within a species, as well as interspecies communication among different bacteria. The exptl. detection of AHLs is important in the identification of quorum sensing capabilities in bacteria. Chromobacterium violaceum is a Gram-neg. bacterium that produces the purple pigment violacein in response to the presence of the AHL N-hexanoyl homoserine lactone (C6HSL). The mini-Tn5 mutant strain C. violaceum CV0blu is deficient in the prodn. of this signal mol. but retains the ability to synthesize violacein in response to the presence of C6HSL and a variety of other short-chain AHLs. We have developed a quant. bioassay that measures the amt. of violacein produced by this strain in response to the presence of different concns. of various AHL mols. This new assay provides a means of quantifying the amt. of a given AHL present in a bacterial culture and can be used to measure differences in AHL prodn. among different strains or different batch cultures of a given species.

IT **168982-69-2**, N-(3-Oxo)dodecanoyl homoserine lactone
273734-65-9
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(extn. of violacein from Chromobacterium violaceum provides a new quant. bioassay for N-acyl homoserine lactone autoinducers)

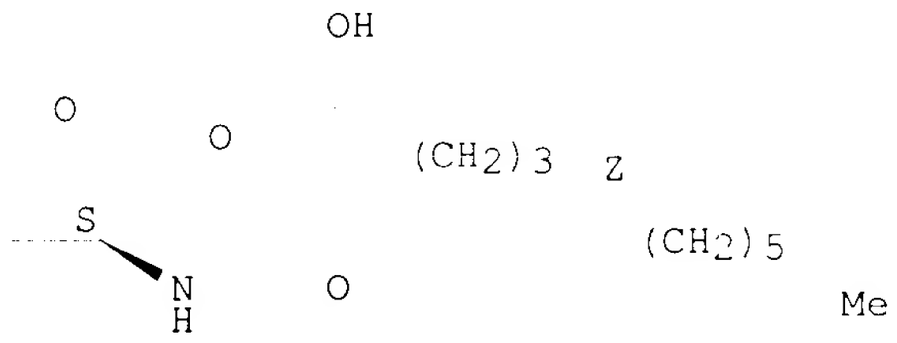
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 273734-65-9 HCAPLUS
CN 7-Tetradecenamide, 3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]-, (7Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

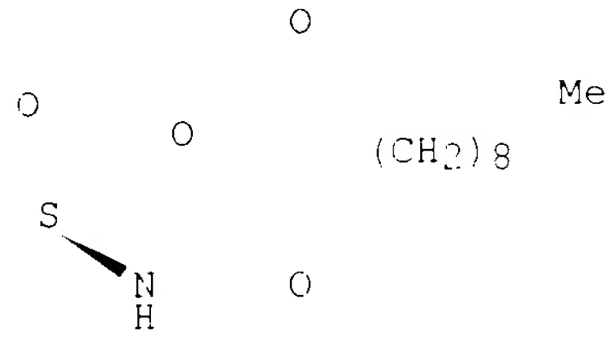
L23 ANSWER 26 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:9749 HCAPLUS
DOCUMENT NUMBER: 132:217886
TITLE: Novel synthetic analogs of the Pseudomonas autoinducer
AUTHOR(S): Kline, T.; Bowman, J.; Iglewski, B. H.; De Kievit, T.; Kakai, Y.; Passador, L.
CORPORATE SOURCE: PathoGenesis Corporation, Seattle, WA, 98119, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(24), 3447-3452
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:217886

AB Release of virulence factors in Pseudomonas **aeruginosa** is regulated by two N-acylhomoserine lactones, PAI-1 and PAI-2, that activate the resp. transcription factors LasR and RhlR. With the goal of developing novel therapeutic agents, we synthesized constrained analogs of PAI-1 and evaluated them in P. **aeruginosa**. Two of the novel analogs bound to LasR and showed agonist activity in LasR stimulation of a lasI-lacZ reporter construct.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(novel synthetic analogs of the Pseudomonas autoinducer)

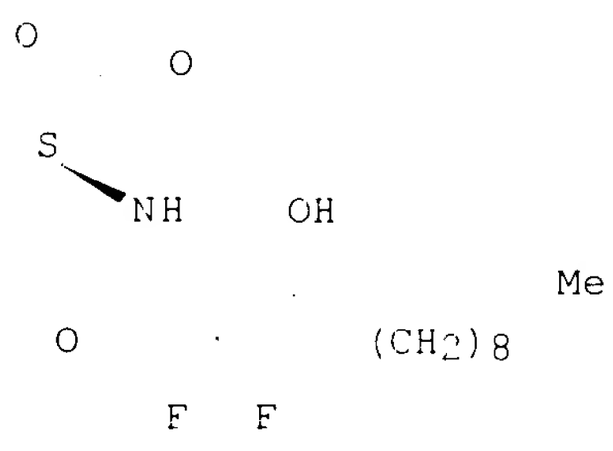
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



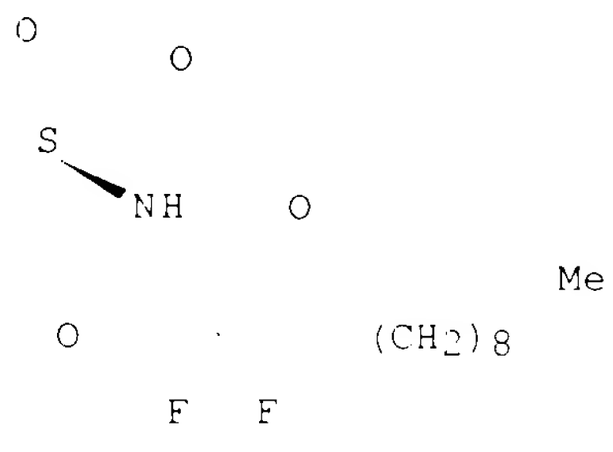
IT **260807-02-1P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(novel synthetic analogs of the Pseudomonas autoinducer)
RN 260807-02-1 HCAPLUS
CN Dodecanamide, 2,2-difluoro-3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **218150-36-8P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(novel synthetic analogs of the Pseudomonas autoinducer)
RN 218150-36-8 HCAPLUS
CN Dodecanamide, 2,2-difluoro-3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Searcher : Shears 308-4994

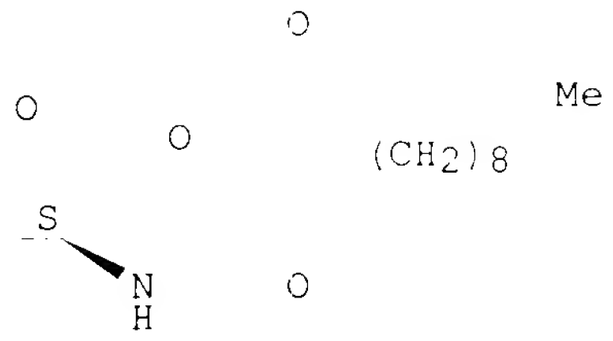
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 27 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:767972 HCAPLUS
DOCUMENT NUMBER: 132:103570
TITLE: Identification of genes controlled by quorum sensing in Pseudomonas **aeruginosa**
AUTHOR(S): Whiteley, Marvin; Lee, Kimberly M.; Greenberg, E. P.
CORPORATE SOURCE: Department of Microbiology, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(24), 13904-13909
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacteria communicate with each other to coordinate expression of specific genes in a cell d.-dependent fashion, a phenomenon called quorum sensing and response. Although we know that quorum sensing via acyl-homoserine lactone (HSL) signals controls expression of several virulence genes in the human pathogen Pseudomonas **aeruginosa**, the no. and types of genes controlled by quorum sensing have not been studied systematically. We have constructed a library of random insertions in the chromosome of a P. **aeruginosa** acyl-HSL synthesis mutant by using a transposon contg. a promoterless lacZ. This library was screened for acyl-HSL induction of lacZ. Thirty-nine quorum sensing-regulated genes were identified. The genes were organized into classes depending on the pattern of regulation. About half of the genes appear to be in seven operons, some seem organized in large patches on the genome. Many of the quorum sensing-regulated genes code for putative virulence factors or prodn. of secondary metabolites. Many of the genes identified showed a high level of induction by acyl-HSL signaling.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(identification, characterization and chromosome mapping of genes controlled by quorum sensing in Pseudomonas **aeruginosa**, high level of induction by acyl-HSL signaling)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 28 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:714186 HCAPLUS
DOCUMENT NUMBER: 132:30331
TITLE: The Pseudomonas **aeruginosa** quorum-sensing signal molecule, N-(3-oxododecanoyl)-L-homoserine lactone, inhibits porcine arterial smooth muscle contraction
AUTHOR(S): Lawrence, R. N.; Dunn, W. R.; Bycroft, B.; Camara, M.; Chhabra, S. R.; Williams, P.; Wilson, V. G.
CORPORATE SOURCE: School of Biomedical Sciences, The Queen's Medical Centre, Nottingham, NG7 2UH, UK
SOURCE: British Journal of Pharmacology (1999), 128(4), 845-848
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

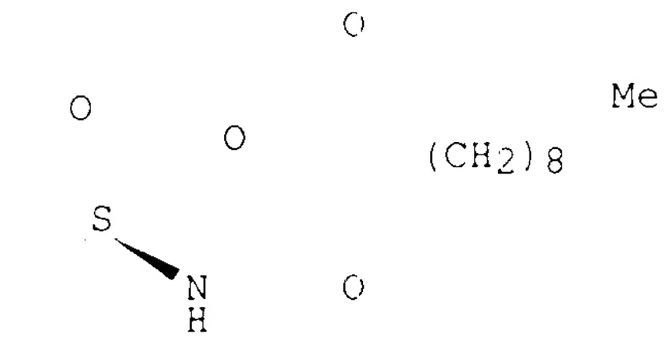
AB The Pseudomonas **aeruginosa** quorum sensing mol. N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) has been shown to suppress cytokine prodn. in macrophages. We have examd. the effect of OdDHL and related compds. on constrictor tone of porcine blood vessels. OdDHL (1-30 .mu.M) caused a concn.-dependent inhibition of U46619-induced contractions of the coronary artery through a largely endothelium-independent mechanism, but was markedly less effective in the pulmonary artery. Quant. similar effects to those produced by OdDHL were obsd. with N-(3-oxododecanoyl)-L-homocysteine thiolactone, a thiolactone deriv., while N-3-oxododecanamide, a lactone-free acyl analog, possessed 1/3rd the potency as a vasorelaxant. Neither N-butanoyl-L-homoserine lactone nor L-homoserine lactone (up to 30 .mu.M) were active. Our findings indicate that OdDHL inhibits vasoconstrictor tone of both pulmonary and coronary blood vessels from the pig. The vasorelaxant action of OdDHL appears to be primarily detd. by the N-acyl chain length, with a minor contribution by the homoserine lactone moiety.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
177158-29-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vasodilating effects of (oxododecanoyl)homoserine lactone and analogs on porcine arterial smooth muscle contraction)

Searcher : Shears 308-4994

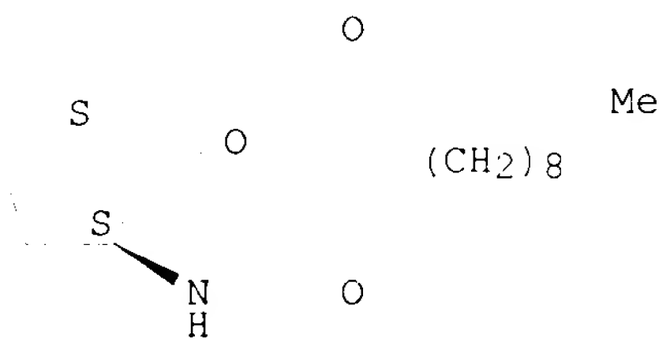
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177158-29-1 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-thienyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 29 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:681880 HCAPLUS
DOCUMENT NUMBER: 132:31556
TITLE: A second operator is involved in Pseudomonas **aeruginosa** elastase (lasB) activation
AUTHOR(S): Anderson, Ronda M.; Zimprich, Chad A.; Rust, Lynn
CORPORATE SOURCE: Department of Veterinary and Microbiological Sciences, North Dakota State University, Fargo, ND, 58105, USA
SOURCE: Journal of Bacteriology (1999), 181(20), 6264-6270
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pseudomonas **aeruginosa** LasB elastase gene (lasB) transcription is controlled by the two-component quorum-sensing system of LasR, and the autoinducer, 3OC12-HSL (N-3-[oxododecanoyl]homoserine lactone). LasR and 3OC12-HSL-mediated lasB activation requires a functional operator sequence (OP1) in the lasB promoter region. Optimal activation of lasB, however, requires

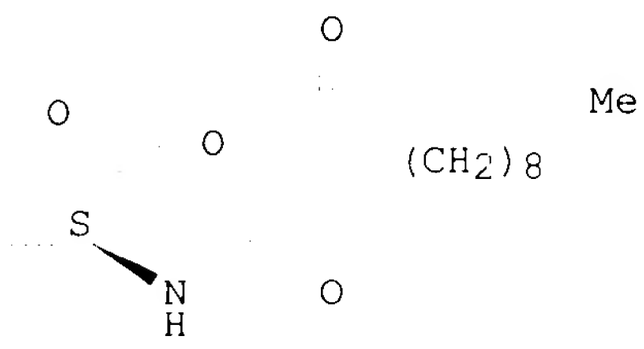
a second sequence of 70% identity to OP1, named OP2, located 43 bp upstream of OP1. In this study, the authors used sequence substitutions and insertion mutations in lasBp-lacZ fusion plasmids to explore the role of OP2 in lasB activation. These results demonstrate that (i) OP1 and OP2 synergistically mediate lasB activation; (ii) OP2, like OP1, responds to LasR and 3OC12-HSL; and (iii) the putative autoinducer-binding domain of LasR is not required for synergistic activation from OP1 and OP2.

IT **168982-69-2**, N-3-[Oxododecanoyl]homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3OC12-HSL regulating OP2 and OP1; second operator is involved in Pseudomonas **aeruginosa** elastase (lasB) activation)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 30 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:651464 HCAPLUS
DOCUMENT NUMBER: 132:276
TITLE: Pseudomonas **aeruginosa** quorum-sensing signal molecule N-(3-oxododecanoyl)-L-homoserine lactone inhibits expression of P2Y receptors in cystic fibrosis tracheal gland cells
AUTHOR(S): Saleh, A.; Figarella, C.; Kammouni, W.; Marchand-Pinatel, S.; Lazdunski, A.; Tubul, A.; Brun, P.; Merten, M. D.
CORPORATE SOURCE: Groupe de Recherche sur les Glandes Exocrines, Faculte de Medecine, Marseille, 13385/05, Fr.
SOURCE: Infection and Immunity (1999), 67(10), 5076-5082
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ATP and UTP have been proposed for use as therapeutic treatment of the abnormal ion transport in the airway epithelium in cystic fibrosis (CF), the most characteristic feature of which is permanent infection by Pseudomonas **aeruginosa**. As for diverse gram-neg. bacteria, this pathogenic bacterium accumulates diffusible N-acylhomoserine lactone (AHL) signal mols., and when a threshold concn. is reached, virulence factor genes are activated. Human

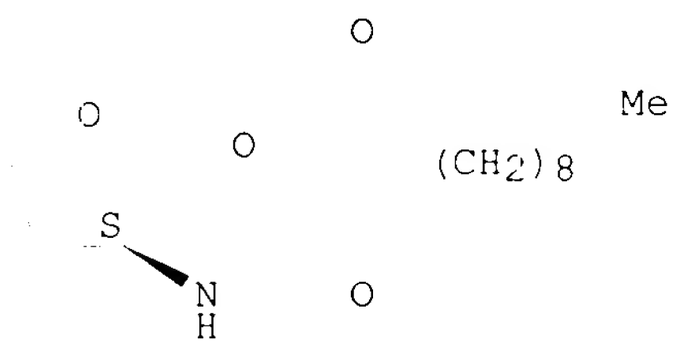
submucosal tracheal gland serous (HTGS) cells are believed to play a major role in the physiopathol. of CF. Since ATP and UTP stimulate CF epithelial cells through P2Y receptors, we sought to det. whether CF HTGS cells are capable of responding to the AHLs N-butanoyl-L-homoserine lactone (BHL), N-hexanoyl-L-homoserine lactone (HHL), N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL), and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL), with special ref. to P2Y receptors. All AHLs inhibited ATP- and UTP-induced secretion by CF HTGS cells. The 50% inhibitory concns. were as high as 10 and 5 .mu.M for BHL and HHL, resp., but were only 0.3 and 0.4 pM for OdDHL and OHHL, resp. Furthermore, all AHLs down-regulated the expression of the P2Y2 and P2Y4 receptors. Ibuprofen and nordihydroguaiaretic acid were able to prevent AHL inhibition of the responses to nucleotides, but neither dexamethasone nor indomethacin was able to do this. These data indicate that AHLs may alter responsiveness to ATP and UTP by CF HTGS cells and suggest that, in addn. to ATP and/or UTP analogs, ibuprofen may be of use for a combinational pharmacol. therapy for CF.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Pseudomonas **aeruginosa** quorum-sensing N-acylhomoserine lactone signal mols. inhibit expression of P2Y receptors in cystic fibrosis tracheal gland cells and effects of ATP-UTP and ibuprofen)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 31 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:149906 HCAPLUS
DOCUMENT NUMBER: 130:293770
TITLE: Active efflux and diffusion are involved in transport of Pseudomonas **aeruginosa** cell-to-cell signals
AUTHOR(S): Pearson, James P.; Van Delden, Christian; Iglewski, Barbara H.
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Bacteriology (1999), 181(4), 1203-1210

Searcher : Shears 308-4994

CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

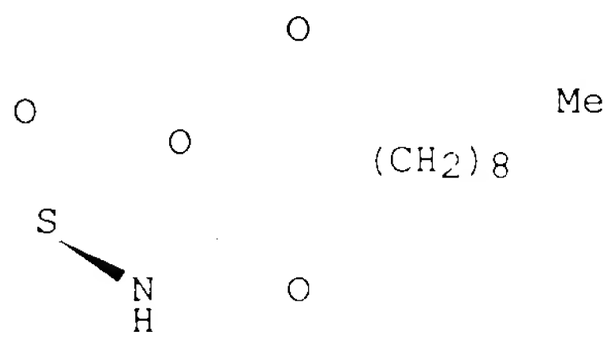
AB Many gram-neg. bacteria communicate by N-acyl homoserine lactone signals called autoinducers (AIs). In Pseudomonas **aeruginosa**, cell-to-cell signaling controls expression of extracellular virulence factors, the type II secretion app., a stationary-phase sigma factor (.sigma.s), and biofilm differentiation. The fact that a similar signal, N-(3-oxohexanoyl) homoserine lactone, freely diffuses through Vibrio fischeri and Escherichia coli cells has led to the assumption that all AIs are freely diffusible. In this work, transport of the two P. **aeruginosa** AIs, N-(3-oxododecanoyl) homoserine lactone (3OC12-HSL) (formerly called PAI-1) and N-butyryl homoserine lactone (C4-HSL) (formerly called PAI-2), was studied by using tritium-labeled signals. When [3H]C4-HSL was added to cell suspensions of P. **aeruginosa**, the cellular concn. reached a steady state in less than 30 s and was nearly equal to the external concn., as expected for a freely diffusible compd. In contrast, [3H]3OC12-HSL required about 5 min to reach a steady state, and the cellular concn. was 3 times higher than the external level. Addn. of inhibitors of the cytoplasmic membrane proton gradient, such as azide, led to a strong increase in cellular accumulation of [3H]3OC12-HSL, suggesting the involvement of active efflux. A defined mutant lacking the mexA-mexB-oprM-encoded active-efflux pump accumulated [3H]3OC12-HSL to levels similar to those in the azide-treated wild-type cells. Efflux expts. confirmed these observations. Our results show that in contrast to the case for C4-HSL, P. **aeruginosa** cells are not freely permeable to 3OC12-HSL. Instead, the mexA-mexB-oprM-encoded efflux pump is involved in active efflux of 3OC12-HSL. Apparently the length and/or degree of substitution of the N-acyl side chain dets. whether an AI is freely diffusible or is subject to active efflux by P. **aeruginosa**.

IT **168982-69-2**, N-(3-Oxododecanoyl) homoserine lactone
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoinducer; active efflux and diffusion are involved in transport of Pseudomonas **aeruginosa** cell-to-cell signals)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE

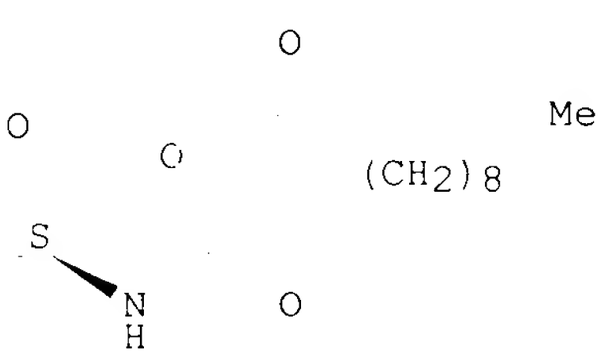
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 32 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:116307 HCAPLUS
DOCUMENT NUMBER: 130:222191
TITLE: Correlation between autoinducers and rhamnolipids production by Pseudomonas **aeruginosa** IFO 3924
AUTHOR(S): Nakata, Kuniho; Yoshimoto, Akihiro; Yamada, Yasuhiro
CORPORATE SOURCE: Central Research Laboratories, Meiji Seika Corporation, Fujisawa, 251-0057, Japan
SOURCE: Journal of Fermentation and Bioengineering (1998), 86(6), 608-610
CODEN: JFBIEX; ISSN: 0922-338X
PUBLISHER: Society for Fermentation and Bioengineering, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High rhamnolipid productivity (32 g/l) was obtained in an ethanol fed-batch culture of Pseudomonas **aeruginosa** IFO 3924. Examn. of the autoinducer level and exogenous autoinducer addn. tests indicated that in the fed-batch system high autoinducer activity, which was about ten-fold that obtained in an unfed system, was thought to be the cause of the high rate of rhamnolipid prodn. Both N-(3-oxohexanoyl)-L-homoserine lactone (OHHL) and N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) enhanced rhamnolipid productivity in the unfed system.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(correlation between autoinducers and rhamnolipids prodn. by Pseudomonas **aeruginosa** IFO 3924)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 33 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:9682 HCAPLUS
DOCUMENT NUMBER: 130:63217
TITLE: Methods and compositions for controlling biofilm development

INVENTOR(S): Davies, David G.; Costerton, John William
PATENT ASSIGNEE(S): The Research and Development Institute, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9857618	A1	19981223	WO 1998-US12695	19980618
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 9858075	A2	19981223	WO 1998-US12718	19980617
WO 9858075	A3	19990318		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9882589	A1	19990104	AU 1998-82589	19980617
EP 994961	A2	20000426	EP 1998-932782	19980617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514092	T2	20020514	JP 1999-504816	19980617
AU 9879776	A1	19990104	AU 1998-79776	19980618
US 6455031	B1	20020924	US 1999-319580	19990609

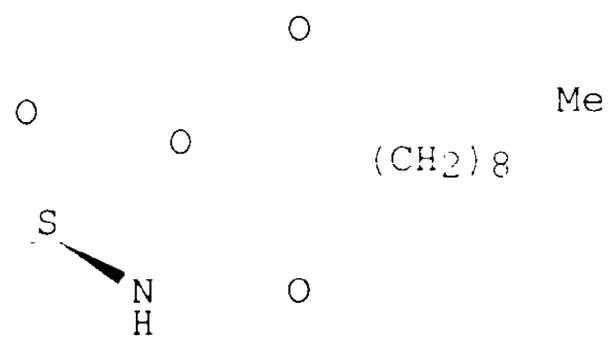
PRIORITY APPLN. INFO.: US 1997-50093P P 19970618
US 1998-98875 A 19980617
WO 1998-US12728 W 19980617
WO 1998-US12695 W 19980618

OTHER SOURCE(S): MARPAT 130:68217

AB A method of cleaning or protecting surfaces by treatment with compns. comprising N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) blocking compds. and/or N-butyryl-L-homoserine lactone (BHL) analogs, either in combination or sep. An example is given to det. the role of homoserine lactone signal mols. on the formation of biofilms by cells of Pseudomonas **aeruginosa**. A liq. general purpose heavy duty cleaner contained Calsuds 81N conc. 2.0-4.0, tetra-K pyrophosphate 5.0-10.0, Na xylenesulfonate (40%) 7.5-12.5% BHL analog 2.5 ppm and water to 100%.

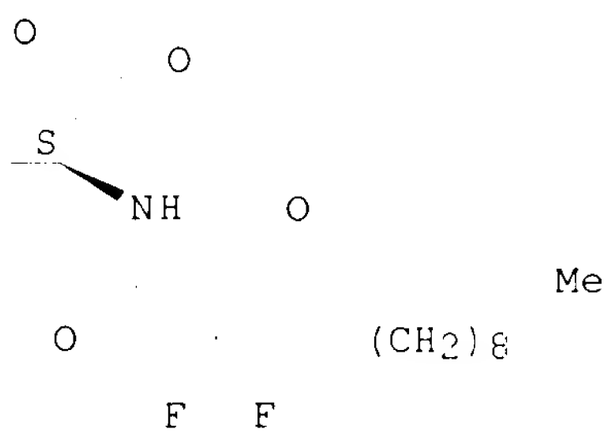
IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study) (blockers; compns. for controlling biofilm development contg. homoserine lactone derivs.)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **218150-36-8**
RL: BUU (Biological use, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)
(compns. for controlling biofilm development contg. homoserine lactone derivs.)
RN 218150-36-8 HCAPLUS
CN Dodecanamide, 2,2-difluoro-3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 34 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:699972 HCAPLUS
DOCUMENT NUMBER: 130:35449
TITLE: Production of acyl-homoserine lactone quorum-sensing signals by Gram-negative plant-associated bacteria
AUTHOR(S): Cha, Chung; Gao, Ping; Chen, Yu-Ching; Shaw, Paul D.; Farrand, Stephen K.
CORPORATE SOURCE: Department of Crop Sciences, University of Illinois at Urbana-Champaign, Urbana, 61801, USA
SOURCE: Molecular Plant-Microbe Interactions (1998), 11(11), 1119-1129
CODEN: MPMIEL; ISSN: 0894-0282
PUBLISHER: APS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many Gram-neg. bacteria regulate expression of specialized gene sets in response to population d. This regulatory mechanism, called autoinduction or quorum-sensing, is based on the prodn. by the bacteria of a small, diffusible signal mol. called the autoinducer.

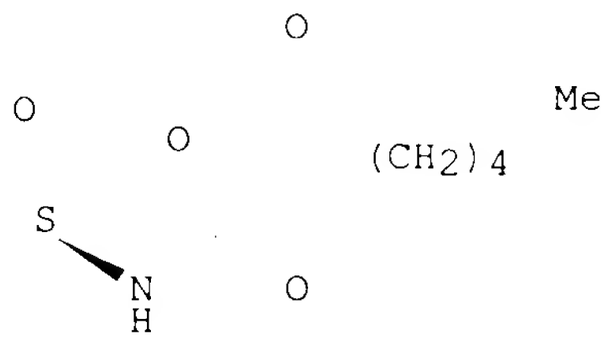
In the most well-studied systems, the autoinducers are N-acylated derivs. of L-homoserine lactone (acyl-HSL). Signal specificity is conferred by the length, and the nature of the substitution at C-3, of the acyl side-chain. The authors evaluated four acyl-HSL bioreporters, based on tra of Agrobacterium tumefaciens, lux of Vibrio fischeri, las of Pseudomonas **aeruginosa**, and pigment prodn. by Chromobacterium violaceum, for their ability to detect sets of 3-oxo acyl-HSLs, 3-hydroxy acyl-HSLs, and alkanoyl-HSLs with chain lengths ranging from C4 to C12. The traG::lacZ fusion reporter from the A. tumefaciens Ti plasmid was the single most sensitive and versatile detector of the four. Using this reporter, the authors screened 106 isolates representing seven genera of bacteria that assoc. with plants. Most of the Agrobacterium, Rhizobium, and Pantoea isolates and about half of the Erwinia and Pseudomonas isolates gave pos. reactions. Only a few isolates of Xanthomonas produced a detectable signal. The authors characterized the acyl-HSLs produced by a subset of the isolates by thin-layer chromatog. Among the pseudomonads and erwinias, most produced a single dominant activity chromatographing with the properties of N-(3-oxo-hexanoyl)-L-HSL. However, a few of the erwinias, and the P. fluorescens and Ralstonia solanacearum isolates, produced quite different signals, including 3-hydroxy forms, as well as active compds. that chromatographed with properties unlike any of the stds. The few pos. xanthomonads, and almost all of the agrobacteria, produced small amts. of a compd. with the chromatog. properties of N-(3-oxo-octanoyl)-L-HSL. Members of the genus Rhizobium showed the greatest diversity, with some producing as few as one and others producing as many as seven detectable signals. Several isolates produced extremely nonpolar compds. indicative of very long acyl side-chains. Prodn. of these compds. suggests that quorum-sensing is common as a gene regulatory mechanism among Gram-neg. plant-assocd. bacteria.

IT **147795-39-9**, N-(3-Oxo-octanoyl)-L-homoserine lactone
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(prodn. of acyl-homoserine lactone quorum-sensing signals by Gram-neg. plant-assocd. bacteria)

RN 147795-39-9 HCAPLUS

CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 35 OF 47 HCAPLUS COPYRIGHT 2002 ACS

Searcher : Shears 308-4994

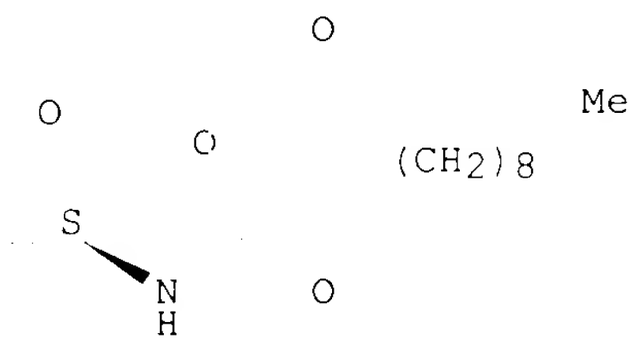
ACCESSION NUMBER: 1998:567853 HCAPLUS
DOCUMENT NUMBER: 129:341534
TITLE: Quorum-sensing and siderophore biosynthesis in Pseudomonas **aeruginosa**: lasR/lasI mutants exhibit reduced pyoverdineb biosynthesis
AUTHOR(S): Stintzi, Alain; Evans, Kelly; Meyer, Jean-Marie; Poole, Keith
CORPORATE SOURCE: Department of Microbiology and Immunology, Queen's University, Kingston, ON, K7L 3N6, Can.
SOURCE: FEMS Microbiology Letters (1998), 166(2), 341-345
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cell d.-dependent gene expression in Pseudomonas **aeruginosa** is controlled, in part, by the quorum-sensing regulator LasR. LasR null mutants exhibited a reproducible 2-fold decrease in prodn. of the catecholate-hydroxamate siderophore pyoverdine during grown under iron-limiting conditions. Similarly, lasI mutants defective in the biosynthesis of the autoinducer PAI-1 also exhibited a 2-fold decrease in pyoverdine prodn. which could be largely restored upon addn. of exogenous PAI-1. LasR mutants were not altered with respect to expression of the pvdD gene involved in the synthesis of the peptide portion of pyoverdine, indicating that some other pyoverdine biosynthetic gene(s) were affected by the LasRI status of the cell. This represents the first report of quorum-sensing regulation of siderophore prodn. in bacteria and highlights the fact that cell d., while not an essential signal for pyoverdine expression, does enhance prodn. of this siderophore.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(quorum-sensing regulation of siderophore biosynthesis in Pseudomonas **aeruginosa** lasR/lasI mutants exhibit reduced pyoverdine biosynthesis)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 36 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:456182 HCAPLUS
DOCUMENT NUMBER: 129:158983
TITLE: Induction of entry into the stationary growth

phase in Pseudomonas **aeruginosa** by N-acylhomoserine lactone

AUTHOR(S): You, Zhiying; Fukushima, Jun; Tanaka, Kan; Kawamoto, Susumu; Okuda, Kenji

CORPORATE SOURCE: Dep. Bacteriology, Yokohama City Univ. Sch. Med., Kanazawa-ku, Yokohama, 236, Japan

SOURCE: FEMS Microbiology Letters (1998), 164(1), 99-106
CODEN: FMLED7; ISSN: 0378-1097

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

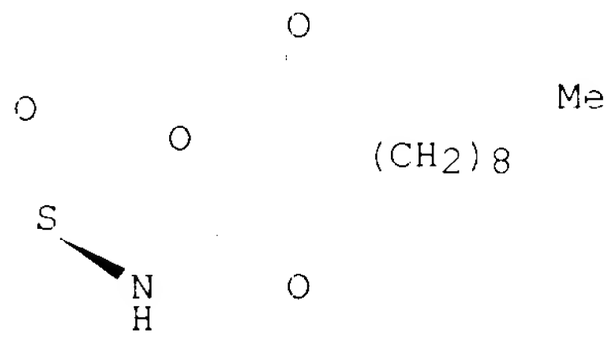
AB N-acylhomoserine lactone (AHSL, autoinducer) is capable of regulating a set of genes by sensing cell d. and developing an intercellular communication in Pseudomonas **aeruginosa**. Addn. of AHSL in the exponential growth phase, regardless of cell d., induces a repression of cell growth of P. **aeruginosa**, an expression of stationary phase specific factor .sigma.s in vivo and a morphol. change into smaller spherical shape indistinguishable from that in the stationary phase. It is demonstrated that AHSL can trigger an entry of bacteria into stationary phase as a growth controlling signal.

IT **168982-69-2**, N-(3-Oxododecanoyl)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(induction of entry into stationary growth phase in Pseudomonas **aeruginosa** by N-acylhomoserine lactone)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 37 OF 47 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:7802 HCAPLUS

DOCUMENT NUMBER: 128:113961

TITLE: The Pseudomonas **aeruginosa** quorum-sensing signal molecule N-(3-oxododecanoyl)-L-homoserine lactone has immunomodulatory activity

AUTHOR(S): Telford, Gary; Wheeler, D.; Williams, Paul; Tomkins, P. T.; Appleby, P.; Sewell, Herbert; Stewart, Gordon S. A. B.; Bycroft, Barrie W.; Pritchard, David I.

CORPORATE SOURCE: Department of Life Science, University of Nottingham, University Park, Nottingham, NG7

Searcher : Shears 308-4994

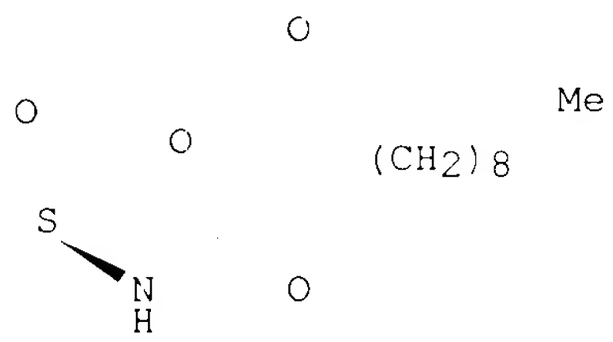
2RD, UK
SOURCE: Infection and Immunity (1998), 66(1), 36-42
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diverse gram-neg. bacterial cells communicate with each other by using diffusible N-acyl homoserine lactone (AHL) signal mols. to coordinate gene expression with cell population d. Accumulation of AHLs above a threshold concn. renders the population "quorate," and the appropriate target gene is activated. In pathogenic bacteria, such as P. **aeruginosa**, AHL-mediated quorum sensing is involved in the regulation of multiple virulence determinants. The authors therefore sought to det. whether the immune system is capable of responding to these bacterial signal mols. Consequently the immunomodulatory properties of the AHLs N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL) were evaluated in murine and human leukocyte immunoassays in vitro. OdDHL, but not OHHL, inhibited lymphocyte proliferation and tumor necrosis factor .alpha.a prodn. by lipopolysaccharide-stimulated macrophages. Furthermore, OdDHL simultaneously and potently down-regulated the prodn. of IL-12, a Th1-supportive cytokine. At high concns. (>7.times.10-5 M) OdDHL inhibited antibody prodn. by keyhole limpet hemocyanin-stimulated spleen cells, but at lower concns. (<7.times.10-5 M), antibody prodn. was stimulated, apparently by increasing the proportion of the IgG1 isotype. OdDHL also promoted IgE prodn. by interleukin-4-stimulated human peripheral blood mononuclear cells. Thus, OdDHL may influence the Th1-Th2 balance in the infected host and, in addn. to regulating the expression of virulence determinants, OdDHL may contribute to the pathogenesis of P. **aeruginosa** infections by functioning as a virulence determinant per se.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Pseudomonas **aeruginosa** quorum-sensing signal mol. L-homoserine lactone has immunomodulatory activity)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 38 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:625337 HCAPLUS
DOCUMENT NUMBER: 127:303989

Searcher : Shears 308-4994

TITLE: Roles of Pseudomonas **aeruginosa** las and rhl quorum-sensing systems in control of elastase and rhamnolipid biosynthesis genes

AUTHOR(S): Pearson, James P.; Pesci, Everett C.; Iglewski, Barbara H.

CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, Rochester, NY, 14642, USA

SOURCE: Journal of Bacteriology (1997), 179(18), 5756-5767
CODEN: JOBAAY; ISSN: 0021-9193

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

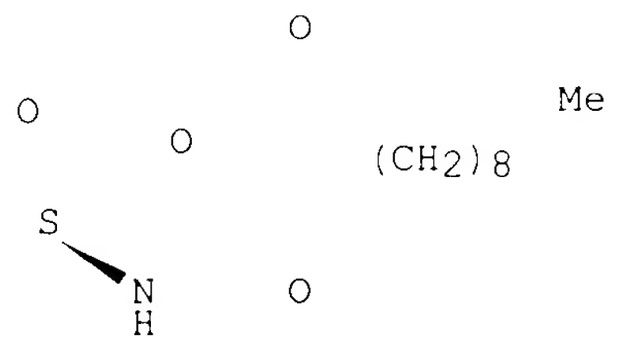
AB Two quorum-sensing systems (las and rhl) regulate virulence gene expression in Pseudomonas **aeruginosa**. The las system consists of a transcriptional activator, LasR, and LasI, which directs the synthesis of the autoinducer N-(3-oxododecanoyl)homoserine lactone (PAI-1). Induction of lasB (encoding elastase) and other virulence genes requires LasR and PAI-1. The rhl system consists of a putative transcriptional activator, RhlR, and RhlI, which directs the synthesis of N-butyryl homoserine lactone (PAI-2). Rhamnolipid prodn. in P. **aeruginosa** has been reported to require both the rhl system and rhlAB (encoding a rhamnosyltransferase). Here we report the generation of a .DELTA.lasI mutant and both .DELTA.lasI .DELTA.rhlI and .DELTA.lasR rhlR.DELTA.Tn501 double mutants of strain PAO1. Rhamnolipid prodn. and elastolysis were reduced in the .DELTA.lasI single mutant and abolished in the double-mutant strains. RhlAB mRNA was not detected in these strains at mid-logarithmic phase but was abundant in the parental strain. Further RNA anal. of the wild-type strain revealed that rhlAB is organized as an operon. The rhlAB transcriptional start was mapped, and putative .sigma.54 and .sigma.70 promoters were identified upstream. To define components required for rhlAB expression, we developed a bioassay in Escherichia coli and demonstrated that PAI-2 and RhlR are required and sufficient for expression of rhlA. To characterize the putative interaction between PAI-2 and RhlR, we demonstrated that [3H]PAI-2 binds to E. coli cells expressing RhlR and not to those expressing LasR. Finally, the specificity of the las and rhl systems was examd. in E. coli bioassays. The las system was capable of mildly activating rhlA, and similarly, the rhl system partly activated lasB. However, these effects were much less than the activation of rhlA by the rhl system and lasB by the las system. The results presented here further characterize the roles of the rhl and las quorum-sensing systems in virulence gene expression.

IT **168982-69-2**, N-(3-Oxododecanoyl) homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(PAI-1; Pseudomonas **aeruginosa** las and rhl quorum-sensing systems in control of elastase and rhamnolipid biosynthesis genes)

RN 168982-69-2 HCAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



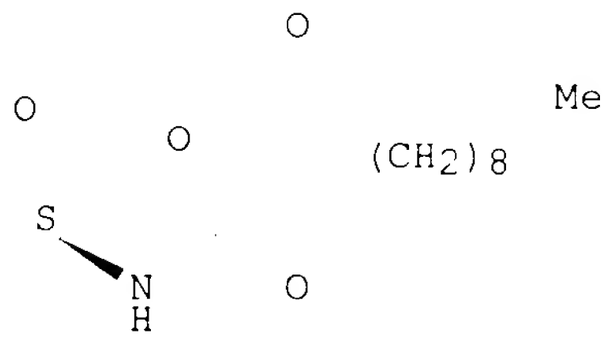
L23 ANSWER 39 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:442322 HCAPLUS
DOCUMENT NUMBER: 127:173757
TITLE: Regulation of the xcp secretion pathway by multiple quorum-sensing modulons in Pseudomonas **aeruginosa**
AUTHOR(S): Chapon-Herve, Virginie; Akrim, Mohammed; Latifi, Amel; Williams, Paul; Lazdunski, Andree; Bally, Marc
CORPORATE SOURCE: Laboratoire d'Ingenierie des Systemes Macromoleculaires, Centre National de la Recherche Scientifique, Marseille, 13402, Fr.
SOURCE: Molecular Microbiology (1997), 24(6), 1169-1178
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The virulence of the opportunistic pathogen Pseudomonas **aeruginosa** is largely dependent upon the extracellular prodn. of a no. of secreted proteins with toxic or degradative activities. The synthesis of several exoenzymes is controlled in a cell-d.-dependent manner by two interlinked quorum-sensing systems. Their secretion across the outer membrane occurs through the Xcp translocation machinery. The xcp locus located at 40 min on the chromosome consists of two divergently transcribed operons, namely xcpPQ and xcpR to xcpZ. In this study, transcriptional fusions were constructed between the xcpP and xcpR genes and the lacZ reporter. Transcriptional activation of the xcpP and xcpR genes in P. **aeruginosa** is growth-phase dependent and the lasR-lasI auto-induction system is required for this control. In the heterologous host Escherichia coli, the lasR gene product, together with its cognate autoinducer N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL), activates both the xcpP-lacZ and the xcpR-lacZ gene fusion. The second P. **aeruginosa** quorum-sensing modulon rhlR-rhlI (vsmR-vsmI) is also involved in the control of the xcp genes. Expression of the lacZ fusions is strongly reduced in PAN067, a pleiotropic mutant defective in the prodn. of N-acyl-homoserine lactones responsible for the activation of RhlR. Furthermore, introduction of the lasR mutation in PAN067 results in addnl. diminution of xcpP transcription, indicating that the two systems can regulate their target genes independently. These data demonstrate that expression of the xcp secretion system depends on a complex regulatory network involving cell-cell signaling which controls prodn. and secretion of virulence-assocd. factors.

IT **168982-69-2**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of the xcp secretion pathway by multiple quorum-sensing modulons in Pseudomonas **aeruginosa**)
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



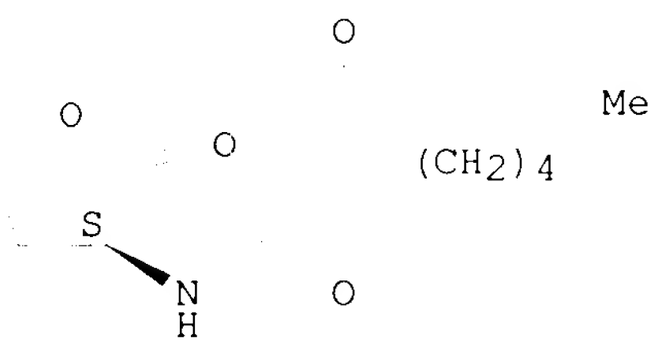
L23 ANSWER 40 OF 47 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:394418 HCAPLUS
DOCUMENT NUMBER: 127:119145
TITLE: Detecting and characterizing N-acyl-homoserine lactone signal molecules by thin-layer chromatography
AUTHOR(S): Shaw, Paul D.; Ping, Gao; Daly, Sean L.; Cha, Chung; Cronan, John E., Jr.; Rinehart, Kenneth L.; Farrand, Stephen K.
CORPORATE SOURCE: Departments Crop Sciences, Chemistry, Microbiology Biochemistry, University Illinois, Urbana, IL, 61801, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(12), 6036-6041
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many Gram-neg. bacteria regulate gene expression in response to their population size by sensing the level of acyl-homoserine lactone signal mols. which they produce and liberate to the environment. We have developed an assay for these signals that couples sepn. by thin-layer chromatog. with detection using Agrobacterium tumefaciens harboring lacZ fused to a gene that is regulated by autoinduction. With the exception of N-butanoyl-L-homoserine lactone, the reporter detected acyl-homoserine lactones with 3-oxo-, 3-hydroxy-, and 3-unsubstituted side chains of all lengths tested. The intensity of the response was proportional to the amt. of the signal mol. chromatographed. Each of the 3-oxo- and the 3-unsubstituted derivs. migrated with a unique mobility. Using the assay, we showed that some bacteria produce as many as five detectable signal mols. Structures could be assigned tentatively on the basis of mobility and spot shape. The dominant species produced by Pseudomonas syringae pv. tabaci chromatographed with the properties of N-(3-oxohexanoyl)-L-homoserine lactone, a structure that was

confirmed by mass spectrometry. An isolate of Pseudomonas fluorescens produced five detectable species, three of which had novel chromatog. properties. These were identified as the 3-hydroxy- forms of N-hexanoyl-, N-octanoyl-, and N-decanoyl-L-homoserine lactone. The assay can be used to screen cultures of bacteria for acyl-homoserine lactones, for quantifying the amts. of these mols. produced, and as an anal. and preparative aid in detg. the structures of these signal mols.

IT **147795-39-9 147795-40-2 168982-69-2 192883-12-8 192883-14-0**
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(detecting and characterizing acylhomoserine lactone signal mols. by thin-layer chromatog.)

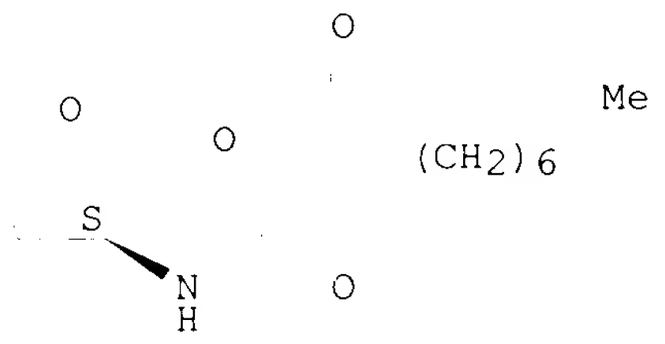
RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



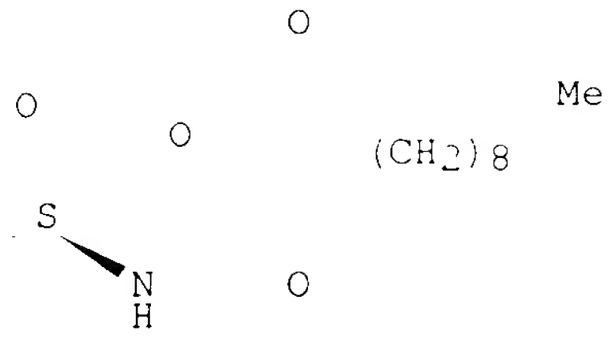
RN 147795-40-2 HCAPLUS
CN Decanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



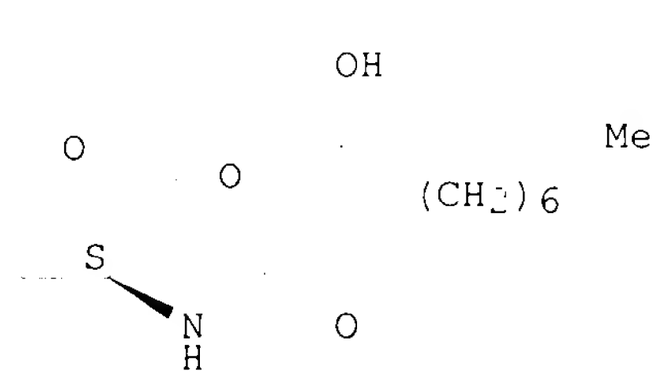
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



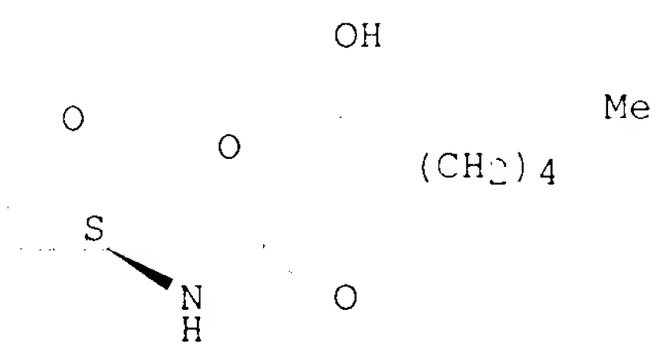
RN 192883-12-8 HCAPLUS
CN Decanamide, 3-hydroxy-N-(tetrahydro-2-oxo-3-furanyl)-, (3S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 192883-14-0 HCAPLUS
CN Octanamide, 3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 41 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:49297 HCAPLUS
DOCUMENT NUMBER: 126:155048
TITLE: Autoinducer molecule
INVENTOR(S): Pearson, James P.; Gray, Kendall M.; Passador, Luciano; Tucker, Kenneth D.; Eberhard, Anatol; Iglewski, Barbara H.; Greenberg, Everett P.
PATENT ASSIGNEE(S): The University of Iowa Research Foundation, USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5591872	A	19970107	US 1993-104487	19930809
US 6057288	A	20000502	US 1995-456864	19950601

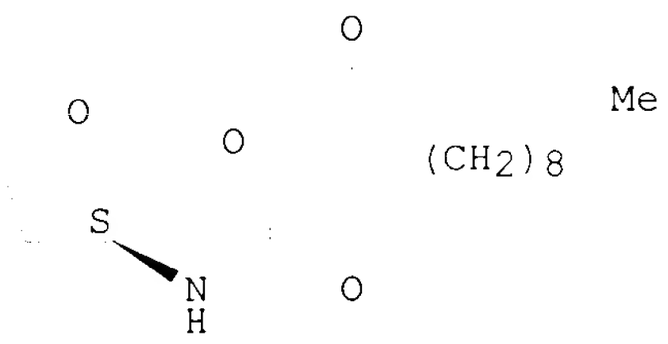
PRIORITY APPLN. INFO.: US 1993-104487 19930809
OTHER SOURCE(S): MARPAT 126:155048

AB Autoinducer mols., e.g., N-(3-oxododecanoyl)homoserine lactone, for Pseudomonas **aeruginosa** are described. The mols. regulate gene expression in the bacterium. Therapeutic compns. and therapeutic methods involving analogs and/or inhibitors of the autoinducer mols. also are described. The mols. are useful for treating or preventing infection by Pseudomonas **aeruginosa**
.

IT **168982-69-2P**, N-(3-Oxododecanoyl)homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(autoinducer of Pseudomonas **aeruginosa** useful for preventing infection by Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 42 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:43967 HCAPLUS
DOCUMENT NUMBER: 126:153566
TITLE: Dissection of the promoter/operator region and evaluation of N-acylhomoserine lactone mediated transcriptional regulation of elastase expression in Pseudomonas **aeruginosa**
AUTHOR(S): Fukushima, Jun; Ishiwata, Tetsuyoshi; You, Zhiying; Ishii, Toshinori; Shigematsu, Takashi; Kurata, Minoru; Chikumaru-Fujita, Shizuko; Bycroft, Barrie W.; Stewart, Gordon S. A. B.; Kawamoto, Ssumu; Morihara, Kazuyuki; Williams, Paul; Okuda, Kenji
CORPORATE SOURCE: Department of Bacteriology, Yokohama City University School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama, 236, Japan
SOURCE: FEMS Microbiology Letters (1997), 146(2), 311-318
CODEN: FMLED7; ISSN: 0378-1097

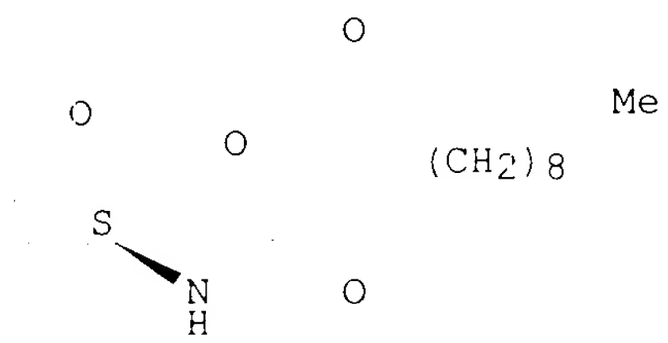
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In Pseudomonas **aeruginosa**, expression of the lasB gene which codes for the metalloprotease, elastase, depends on small diffusible N-acylhomoserine lactones. LasB expression is regulated through the interactions of N-3-oxododecanoyl-L-homoserine lactone and N-butanoyl-L-homoserine lactone with the transcriptional activators LasR and VsmR(RhlR), resp. To investigate lasB expression further, the transcriptional start site was first located to a position 141 bp upstream from the translational start site. Using this information, a series of plasmids were constructed contg. consecutive 5' deletions of the upstream region of lasB fused to a promoterless chloramphenicol acetyltransferase reporter gene. The results obtained indicate that 3 regions are required for efficient transcription of lasB; a 35-bp palindromic sequence located at +26 to +60 bp upstream from the translation start site, and 2 regions located upstream of the transcription start site, at -135 to -85 bp and -63 to -26 bp, resp. Deletion of the latter region results in the loss of both N-butanoyl-L-homoserine lactone- and N-3-oxododecanoyl-L-homoserine lactone-mediated stimulation of lasB expression and provides further support for the role of this operator site as a target for either or both LasR and VsmR.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dissection of the promoter/operator region and evaluation of N-acylhomoserine lactone mediated transcriptional regulation of elastase expression in Pseudomonas **aeruginosa**)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 43 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:617724 HCAPLUS
DOCUMENT NUMBER: 125:267382
TITLE: Functional analysis of the Pseudomonas **aeruginosa** autoinducer PAI
AUTHOR(S): Passador, Luciano; Tucker, Kenneth D.; Guertin, Kevin R.; Journet, Michel P.; Kende, Andrew S.; Iglewski, Barbara H.
CORPORATE SOURCE: Dep. Microbiol. Immunol. Chem., Univ. Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Bacteriology (1996), 178(20), 5995-6000

Searcher : Shears 308-4994

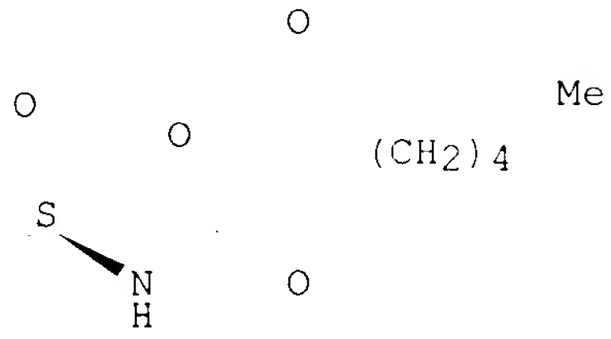
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of structural analogs of the Pseudomonas **aeruginosa** autoinducer [PAI, N-3-oxo-dodecanoyl homoserine lactone] were obtained and tested for their ability to act as autoinducers in stimulating the expression of the gene for elastase (lasB) by measuring .beta.-galactosidase prodn. from a lasB-lacZ gene fusion in the presence of the transcriptional activator LasR. The data suggest that the length of the acyl side chain of the autoinducer mol. is the most crit. factor for activity. Replacement of the ring O by S in the homoserine lactone moiety can be tolerated. Tritium-labeled PAI ([3H]PAI) was synthesized and used to demonstrate the assocn. of [3H]PAI with cells overexpressing LasR. The PAI analogs were also tested for their ability to compete with [3H]PAI for binding of LasR. Results from the competition assays suggest that once again the length of the acyl side chain appears to be crucial for antagonist activity. The presence of the 3-oxo moiety also plays a significant role in binding since analogs which lacked this moiety were much less effective in blocking binding of [3H]PAI. All analogs demonstrating competition with PAI in binding to LasR also exhibited the ability to activate lasB expression, suggesting that they are functional analogs of PAI.

IT **147795-39-9P 147795-40-2P 168982-69-2P**
177158-19-9P 177158-29-1P 182359-59-7P
182359-60-0P 182359-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(N-acylhomoserine lactone analogs and their ability to mimic Pseudomonas **aeruginosa** autoinducer PAI in stimulating LasR-mediated lasB expression)

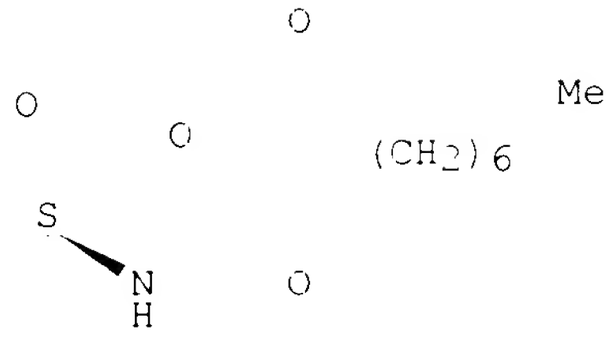
RN 147795-39-9 HCAPLUS
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



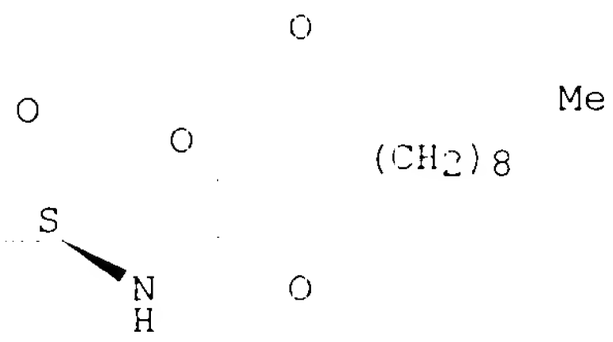
RN 147795-40-2 HCAPLUS
CN Decanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



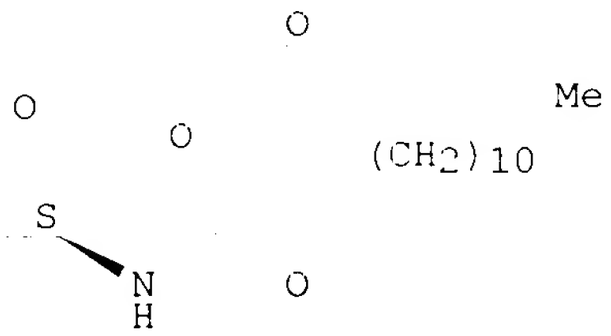
RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



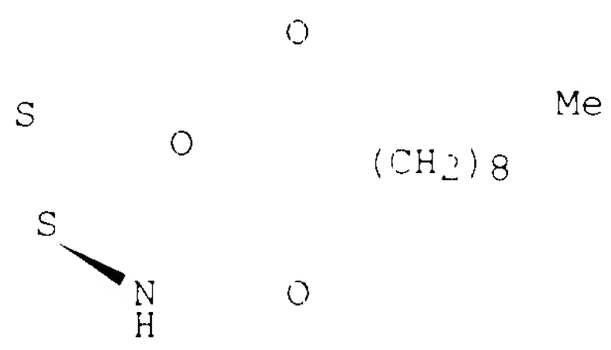
RN 177158-19-9 HCAPLUS
CN Tetradecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177158-29-1 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-thienyl]- (9CI) (CA INDEX NAME)

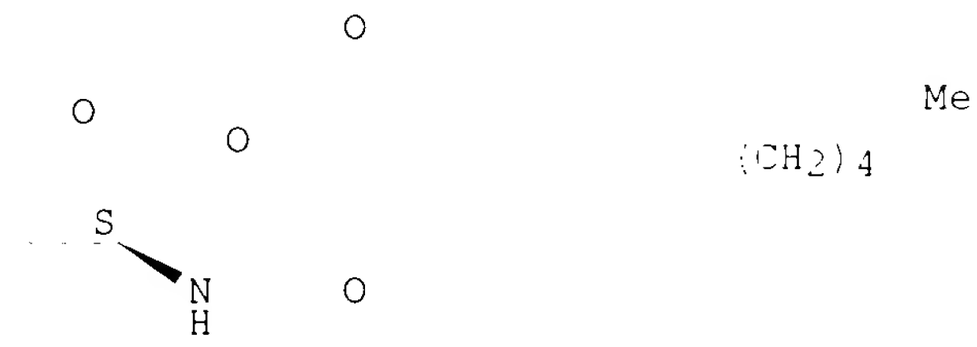
Absolute stereochemistry.



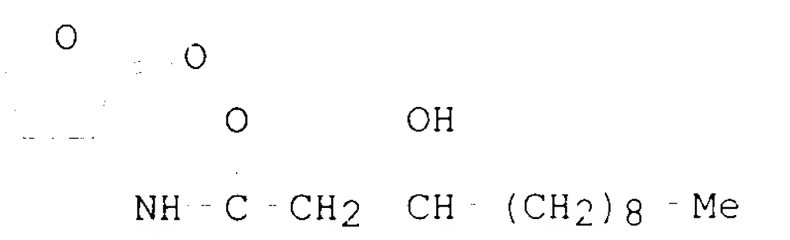
Searcher : Shears 308-4994

RN 182359-59-7 HCAPLUS
CN 6-Dodecenamide, 3-oxo-N-(tetrahydro-2-oxo-3-furanyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

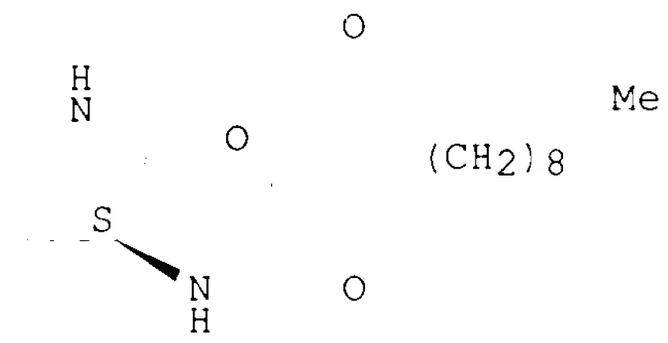


RN 182359-60-0 HCAPLUS
CN Dodecanamide, 3-hydroxy-N-(tetrahydro-2-oxo-3-furanyl)- (9CI) (CA INDEX NAME)



RN 182359-64-4 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-2-oxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 44 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:606154 HCAPLUS
DOCUMENT NUMBER: 125:267351
TITLE: A hierarchical quorum-sensing cascade in Pseudomonas **aeruginosa** links the transcriptional activators LasR and RhlR (VsmR) to expression of the stationary-phase sigma factor RpoS
AUTHOR(S): Latifi, A.; Foglino, M.; Tanaka, K.; Williams, P.; Lazdunski, A.
CORPORATE SOURCE: Lab. d'Ingenierie Dynamique Systemes

Searcher : Shears 308-4994

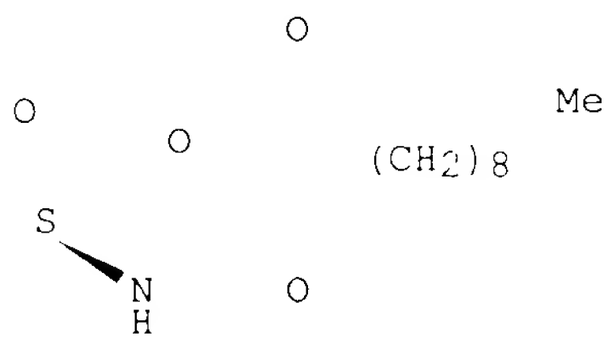
Membranaires, Centre Natl Recherche, Marseille, 13402, Fr.
SOURCE: Molecular Microbiology (1996), 21(6), 1137-1146
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In Pseudomonas **aeruginosa**, the prodn. of many virulence factors and secondary metabolites is regulated in concert with cell d. through quorum sensing. Two quorum-sensing regulons have been identified in which the LuxR homologs LasR and RhlR are activated by N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) and N-butanoyl-L-homoserine lactone (BHL) resp. The lasR and rhlR genes are linked to the luxI homologs lasI and rhlI, which are responsible for synthesis of OdDHL and BHL, resp. As lasRI and rhlRI are both involved in regulating synthesis of exoenzymes such as elastase, the authors sought to det. the nature of their interrelationship. By using lacZ transcriptional fusions in both homologous (P. **aeruginosa**) and heterologous (Escherichia coli) genetic backgrounds the authors provide evidence that (i) lasR is expressed constitutively throughout the growth cycle, (ii) rhlR expression is regulated by LasR/OdDHL, and (iii) that RhlR/BHL regulates rhlI. The authors also show that expression of the stationary-phase sigma factor gene rpoS is abolished in a P. **aeruginosa** lasR mutant and in the pleiotropic BHL-neg. mutant PAN067. Furthermore, the data reveal that in E. coli, an rpoS-lacZ fusion is regulated directly by RhlR/BHL. Taken together, these results indicate that P. **aeruginosa** employs a multilayered hierarchical quorum-sensing cascade involving RhlR/BHL and LasR/OdDHL, interlinked via RpoS, to integrate the regulation of virulence determinants and secondary metabolites with adaptation and survival in the stationary phase.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(a hierarchical quorum-sensing cascade in Pseudomonas **aeruginosa** links the transcriptional activators LasR and RhlR (VsmR) to expression of the stationary-phase sigma factor RpoS)

RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 45 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:36134 HCAPLUS

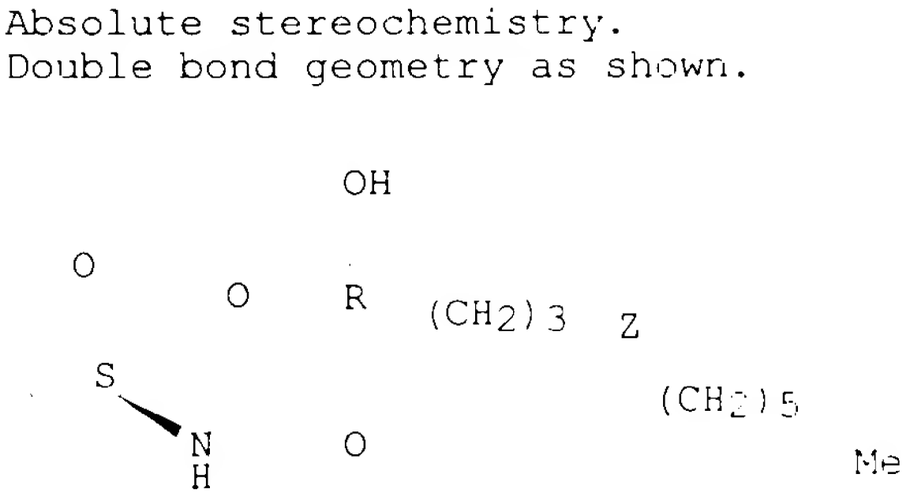
DOCUMENT NUMBER: 124:81661
TITLE: Bacteriocin small of Rhizobium leguminosarum belongs to the class of N-acyl-L-homoserine lactone molecules, known as autoinducers and as quorum sensing co-transcription factors
AUTHOR(S): Schripsema, Jan; de Rudder, Karel E. E.; van Vliet, Theo B.; Lankhorst, Peter P.; de Vroom, Erik; Kijne, Jan W.; van Brussel, Anton A. N.
CORPORATE SOURCE: Div. Pharmacognosy, Gorlaeus Lab., Delft, Neth.
SOURCE: Journal of Bacteriology (1996), 178(2), 366-71
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Small bacteriocin was isolated from the culture broth of the Gram-neg. bacterium Rhizobium leguminosarum, which forms symbiotic nitrogen-fixing root nodules on a no. of leguminous plants. The structure of the mol. was elucidated by spectroscopic methods and identified as N-(3R-hydroxy-7-cis-tetradecanoyl)-L-homoserine lactone. The abs. configuration of both asym. carbon atoms in the mol. was detd. by the use of the chiral solvating agents S-(+)- and R-(-)-2,2,2-trifluoro-1-(9-anthryl)-ethanol. Small bacteriocin is structurally related to the quorum sensing co-transcription factors for genes from other bacteria, such as Vibrio fischeri, Pseudomonas **aeruginosa**, Erwinia carotovora, and Agrobacterium tumefaciens, which are involved in animal-microbe or plant-microbe interactions. The mechanism of regulation of such interactions by this kind of co-transcription factors is still unknown in R. leguminosarum.

IT **172617-17-3P**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(bacteriocin of Rhizobium leguminosarum belongs to class of N-acyl-L-homoserine lactone mols. known as autoinducers and as quorum sensing co-transcription factors)

RN 172617-17-3 HCAPLUS
CN 7-Tetradecenamide, 3-hydroxy-N-[(3S)-tetrahydro-2-oxo-3-furanyl]-, (3R,7Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L23 ANSWER 46 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:841696 HCAPLUS
DOCUMENT NUMBER: 123:250888
TITLE: Multiple N-acyl-L-homoserine lactone signal

Searcher : Shears 308-4994

molecules regulate production of virulence determinants and secondary metabolites in Pseudomonas **aeruginosa**

AUTHOR(S): Winson, Michael K.; Camara, Miguel; Latifi, Amel; Foglino, Maryline; Chhabra, Siri Ram; Daykin, Mavis; Bally, Marc; Chapon, Virginie; Salmond, George P. C.; et al.

CORPORATE SOURCE: Dep. Applied Biochemistry and Food Science, Univ. Nottingham, Leicestershire, LE12 5RD, UK

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(20), 9427-31
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

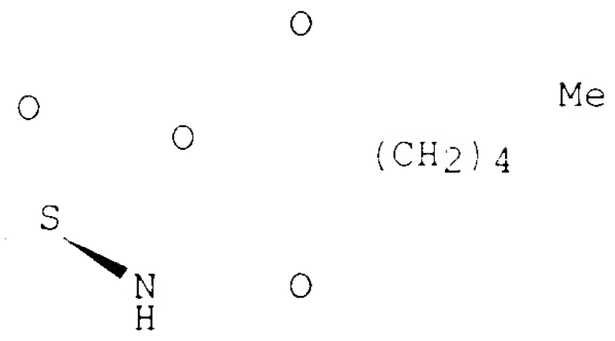
AB P. **aeruginosa** produces a spectrum of exoproducts, many of which have been implicated in the pathogenesis of human infection. Expression of some of these factors requires cell-cell communication involving the interaction of a small diffusible mol., an autoinducer, with a pos. transcriptional activator. In P. **aeruginosa** PAO1, LasI directs the synthesis of the autoinducer N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL), which activates the pos. transcriptional activator, LasR. Recently, a 2nd signaling mol.-based modulon in PAO1, termed vsm, was discovered, which contains the genes vsmR and vsmI. Using HPLC, mass spectrometry, and NMR spectroscopy it was here established that in Escherichia coli, VsmI directs the synthesis of N-butanoyl-L-homoserine lactone (I) and N-hexanoyl-L-homoserine lactone (II). These compds. are present in the spent culture supernatants of P. **aeruginosa** in a molar ratio of .apprxeq.15:1 and their structures were unequivocally confirmed by chem. synthesis. Addn. of either I or II to PAN067, a pleiotropic P. **aeruginosa** mutant unable to synthesize either of these autoinducers, restored elastase, chitinase, and CN- prodn. In E. coli carrying a vsmR/vsmI'::lux transcriptional fusion, I and II activated VsmR to a similar extent. Analogs of these N-acyl-L-homoserine lactones in which the N-acyl side chain has been extended and/or oxidized at the C-3 position exhibit substantially lower activity (e.g., OdDHL) or no activity (e.g., dDHL) in this lux reporter assay. These data indicate that multiple families of quorum-sensing modulons interactively regulate gene expression in P. **aeruginosa**.

IT **147795-39-9 168982-69-2**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(structure-activity relations in acylhomoserine lactone-mediated activation of transcription factor VsmR)

RN 147795-39-9 HCAPLUS

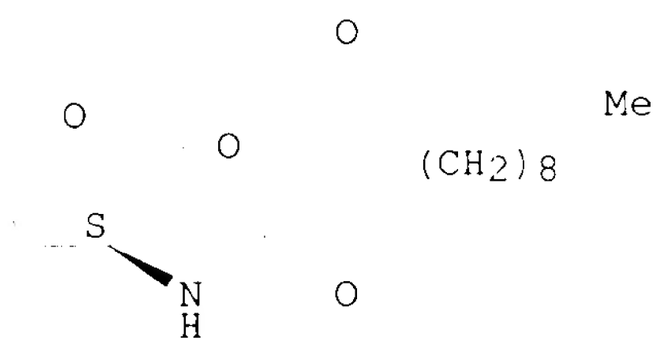
CN Octanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168982-69-2 HCAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

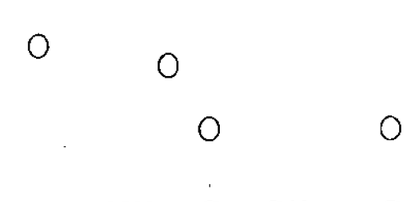


L23 ANSWER 47 OF 47 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:98124 HCAPLUS
DOCUMENT NUMBER: 120:98124
TITLE: Structure of the autoinducer required for expression of Pseudomonas **aeruginosa** virulence genes
AUTHOR(S): Pearson, James P.; Gray, Kendall M.; Passador, Luciano; Tucker, Kenneth D.; Eberhard, Anatol; Iglewski, Barbara H.; Greenberg, E. P.
CORPORATE SOURCE: Dep. Microbiol., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(1), 197-201
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Pseudomonas **aeruginosa** the LasR protein is required for activation of lasB and several other virulence genes. A diffusible signal mol., the P. **aeruginosa** autoinducer (PAI), produced by the bacterial cell and released into the growth medium, is required for activity of LasR. By cloning a lasB::lazZ fusion and a lasR gene under control of the lac promoter in Escherichia coli, the authors have developed a quant. bioassay for PAI. The authors have used this assay to follow the purifn. of PAI from cell-free culture supernatant fluids in which P. **aeruginosa** or E. coli contg. the P. **aeruginosa** gene required for autoinducer synthesis, lasI, had been grown. Chem. analyses indicated the purified material was 3-oxo-N-(tetrahydro-2-oxo-3-furanyl)dodecanamide. To confirm this assignment, the compd. was

synthesized and the synthetic compd. was shown to have chem. and biol. properties identical to those of PAI purified from culture supernatant fluids. The elucidation of the PAI structure suggests therapeutic approaches toward control of P. **aeruginosa** infections.

IT **152833-54-0**
RL: PROC (Process)
(as autoinducer mol. required for activity of LasR in virulence gene expression in Pseudomonas **aeruginosa**, identification of)

RN 152833-54-0 HCAPLUS
CN Dodecanamide, 3-oxo-N-(tetrahydro-2-oxo-3-furanyl)- (9CI) (CA INDEX NAME)



FILE 'REGISTRY' ENTERED AT 14:32:42 ON 22 NOV 2002
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FILE 'CAOLD' ENTERED AT 14:33:07 ON 22 NOV 2002
L25 0 S L24

FILE 'USPATFULL' ENTERED AT 14:33:13 ON 22 NOV 2002
L26 5 S L24

L26 ANSWER 1 OF 5 USPATFULL
ACCESSION NUMBER: 2002:246357 USPATFULL
TITLE: Methods and compositions for controlling biofilm development
INVENTOR(S): Davies, David G, 703 S. 11th Ave., Bozeman, MT, United States 59715
Costerton, John W, 1206 Brentwood Ave., Bozeman, MT, United States 59718

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6455031	B1	20020924	
	WO 9857618		19981223	
APPLICATION INFO.:	US 1999-319580		19990609	(9)
	WO 1998-US12695		19980618	
			19990609	PCT 371 date

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-50093P	19970618	(60)

Searcher : Shears 308-4994

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Ketter, James
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP, Lauro, Esq., Peter C., Hanley, Esq, Elizabeth A.
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1382
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of cleaning or protecting surfaces by treatment with compositions comprising N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) blocking compounds and/or N-butyryl-L-homoserine lactone (BHL) analogs, either in combination or separately.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L26 ANSWER 2 OF 5 USPATFULL
ACCESSION NUMBER: 2002:122261 USPATFULL
TITLE: Immunogenic conjugates of Gram-negative bacterial autoinducer molecules
INVENTOR(S): Kende, Andrew S., Pittsford, NY, United States
Iglewski, Barbara H., Fairport, NY, United States
Smith, Roger, Rochester, NY, United States
Phipps, Richard P., Pittsford, NY, United States
Pearson, James P., Fremont, CA, United States
PATENT ASSIGNEE(S): University of Rochester, Rochester, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6395282	B1	20020528	
APPLICATION INFO.:	US 1999-293687		19990416	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-82025P	19980416 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Devi, S.
LEGAL REPRESENTATIVE: Nixon Peabody LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1633
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an immunogenic conjugate comprising a carrier molecule coupled to an autoinducer of a Gram negative bacteria. The immunogenic conjugate, when combined with a pharmaceutically acceptable carrier, forms a suitable vaccine for mammals to prevent infection by the Gram negative bacteria. The immunogenic conjugate is also used to raise and subsequently isolate antibodies or binding portions thereof which are capable of recognizing and binding to the autoinducer. The antibodies or binding portions thereof are utilized in a method of treating infections, a method of inhibiting autoinducer activity, and in diagnostic assays which detect the presence of autoinducers or autoinducer antagonists in fluid or tissue samples.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L26 ANSWER 3 OF 5 USPATFULL
ACCESSION NUMBER: 2002:6015 USPATFULL
TITLE: Autoinducer compounds
INVENTOR(S): Livinghouse, Tom, Bozeman, MT, United States
PATENT ASSIGNEE(S): The Research & Development Institute, Inc., Bozeman, MT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6337347	B1	20020108	
APPLICATION INFO.:	US 1998-99196		19980618	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Ketter, James
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP, Lauro, Esq., Peter C., Hanley, Esq, Elizabeth A.
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 791
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Autoinducer compounds which enhance gene expression in a wide variety of microorganisms, therapeutic compositions and therapeutic methods wherein gene expression within microorganisms is regulated are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L26 ANSWER 4 OF 5 USPATFULL
ACCESSION NUMBER: 2000:34071 USPATFULL
TITLE: Autoinducer molecule
INVENTOR(S): Pearson, James P., Iowa City, IA, United States
Gray, Kendall M., Iowa City, IA, United States
Passador, Luciano, Rochester, NY, United States
Tucker, Kenneth D., Germantown, MD, United States
Eberhard, Anatol, Brooktondale, NY, United States
Iglewski, Barbara H., Fairport, NY, United States
Greenberg, Everett P., Iowa City, IA, United States
PATENT ASSIGNEE(S): University of Iowa, Iowa City, IA, United States (U.S. corporation)
University of Rochester, Rochester, NY, United States (U.S. corporation)
Ithaca College, Ithaca, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6057288		20000502	
APPLICATION INFO.:	US 1995-456864		19950601	(8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1993-104487, filed on 9 Aug 1993, now patented, Pat. No. US 5591872			

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Minnifield, Nita

Searcher : Shears 308-4994

ASSISTANT EXAMINER: Baskar, Padma
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP, Hanley, Esq., Elizabeth A., Lauro, Esq., Peter C.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 979
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Autoinducer molecules, e.g., N-(3-oxododecanoyl)homoserine lactone, for Pseudomonas aeruginosa are described. The molecules regulate gene expression in the bacterium. Therapeutic compositions and therapeutic methods involving analogs and/or inhibitors of the autoinducer molecules also are described. The molecules are useful for treating or preventing infection by Pseudomonas aeruginosa.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L26 ANSWER 5 OF 5 USPATFULL
ACCESSION NUMBER: 97:1591 USPATFULL
TITLE: Autoinducer molecule
INVENTOR(S): Pearson, James P., Iowa City, IA, United States
Gray, Kendall M., Iowa City, IA, United States
Passador, Luciano, Rochester, NY, United States
Tucker, Kenneth D., Germantown, MD, United States
Eberhard, Anatol, Brooktondale, NY, United States
Iglewski, Barbara H., Fairport, NY, United States
Greenberg, Everett P., Iowa City, IA, United States
PATENT ASSIGNEE(S): The University of Iowa Research Foundation, Iowa City, IA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5591872		19970107	
APPLICATION INFO.:	US 1993-104487		19930309	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Trinh, Ba Kim
LEGAL REPRESENTATIVE: Hanley, Elizabeth A.Lahive & Cockfield
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1,2,3
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1006
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Autoinducer molecules, e.g., N-(3-oxododecanoyl)homoserine lactone, for Pseudomonas aeruginosa are described. The molecules regulate gene expression in the bacterium. Therapeutic compositions and therapeutic methods involving analogs and/or inhibitors of the autoinducer molecules also are described. The molecules are useful for treating or preventing infection by Pseudomonas aeruginosa.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

FILE 'REGISTRY' ENTERED AT 14:35:09 ON 22 NOV 2002
L28 1 SEA FILE=REGISTRY ABB=ON PLU=ON "N-(3-OXODODECANOYL)HOMOSERINE LACTONE"/CN

Searcher : Shears 308-4994

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=> d ide

L28  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   168982-69-2  REGISTRY
CN   Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   Dodecanamide, 3-oxo-N-(tetrahydro-2-oxo-3-furanyl)-, (S)-
OTHER NAMES:
CN   n-(3-Oxododecanoyl) L-homoserine lactone
CN   N-(3-Oxododecanoyl)homoserine lactone
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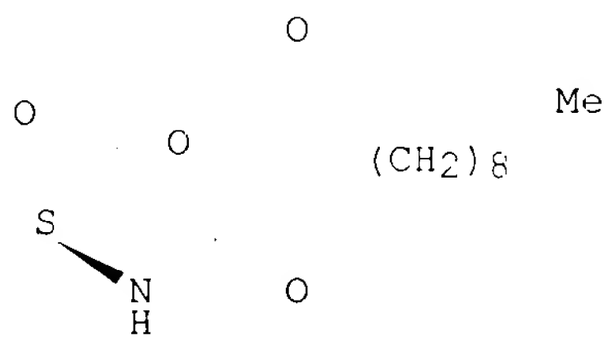
Absolute stereochemistry.

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             55 REFERENCES IN FILE CA (1962 TO DATE)
             56 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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L28            1 S E3

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                 DECANOYL?)(3W)LACTONE
L31           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (3O OR 3(W)(OXO OR
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                 )
L32           56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L29 OR L31) AND
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L33           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND INHIBIT?


L34            5 L33 NOT L23

L34  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:618060  HCAPLUS
```

-key terms

TITLE: Discovery of antagonists of quorum sensing in Pseudomonas **aeruginosa** by combinatorial chemistry and high-throughput screening

AUTHOR(S): Bu, Yigong; Smith, Kristina; Suga, Hiro-aki
CORPORATE SOURCE: Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, NY, 14260-3000, USA

SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-208. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Pseudomonas **aeruginosa** is a gram-neg. bacterium that causes chronic lung infections in approx. 90% of the cystic fibrous patients. This bacterium uses quorum sensing (cell d. sensing) mechanism (which is based on the regulatory protein-autoinducer interaction) to regulate the prodn. of numerous virulence factors and the formation of biofilm. The antagonists of regulatory proteins (LasR and RhlR) are required to stop quorum sensing cascade. Combinatorial chem. was employed for the synthesis of the analogs of the autoinducer [**N-(3-oxododecanoyl**)-L-homoserine **lactone**]. This included the grouped libraries prepd. in the soln. phase and the parallel synthesis performed on the solid phase. The screening revealed three strong agonists and eight weak antagonists of LasR. The SAR studies based on these active mols. allowed us to convert the agonists to potent antagonists of LasR and RhlR. The combination of these potent antagonists indicated strong **inhibition** of the quorum sensing system.

L34 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:484327 HCAPLUS

TITLE: Lysophosphatidic acid **inhibition** of the accumulation of Pseudomonas **aeruginosa** PAO1 alginate, pyoverdin, elastase and LasA

AUTHOR(S): Laux, David C.; Corson, Joy M.; Givskov, Michael; Hentzer, Morten; Moller, Annette; Wosencroft, Kathleen A.; Olson, Joan C.; Krogfelt, Karen A.; Goldberg, Joanna B.; Cohen, Paul S.
CORPORATE SOURCE: Department of Cell and Molecular Biology, University of Rhode Island, Kingston, RI, 02881, USA

SOURCE: Microbiology (Reading, United Kingdom) (2002), 148(6), 1709-1723
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English.

AB The pathogenesis of Pseudomonas **aeruginosa** is at least partially attributable to its ability to synthesize and secrete the siderophore pyoverdin and the two zinc metalloproteases elastase and LasA, and its ability to form biofilms in which bacterial cells are embedded in an alginate matrix. In the present study, a

lysophospholipid, 1-palmitoyl-2-hydroxy-sn-glycero-3-phosphate [also called monopalmitoylphosphatidic acid (MPPA)], which accumulates in inflammatory exudates, was shown to **inhibit** the extracellular accumulation of P. **aeruginosa** PAO1 alginate, elastase, LasA protease and the siderophore pyoverdin. MPPA also **inhibited** biofilm formation. The **inhibitory** effects of MPPA occur independently of rpoS expression and without affecting the accumulation of the autoinducers **N-(3-oxododecanoyl)** homoserine **lactone** and N-butyryl-L-homoserine lactone, and may be due, at least in part, to the ability of MPPA to bind divalent cations.

IT INDEXING IN PROGRESS

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:729021 HCAPLUS
DOCUMENT NUMBER: 136:17770
TITLE: Interference with Pseudomonas quinolone signal synthesis **inhibits** virulence factor expression by Pseudomonas **aeruginosa**
AUTHOR(S): Calfee, M. Worth; Coleman, James P.; Pesci, Everett C.
CORPORATE SOURCE: Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, NC, 27858, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(20), 11633-11637
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB P. **aeruginosa** is an opportunistic pathogen that controls numerous virulence factors through intercellular signals. This bacterium has 2 quorum-sensing systems (las and rhl), which act through the intercellular signals **N-(3-oxododecanoyl)**-L-homoserine **lactone** (**3-oxo-C12-HSL**) and N-butyryl-L-homoserine lactone (C4-HSL), resp. P. **aeruginosa** also produces a 3rd intercellular signal that is involved in virulence factor regulation. This signal, 2-heptyl-3-hydroxy-4-quinolone [referred to as the Pseudomonas quinolone signal (PQS)], is a secondary metabolite that is part of the P. **aeruginosa** quorum-sensing hierarchy. PQS can induce both lasB (encodes LasB elastase) and rhlI (encodes the C4-HSL synthase) in P. **aeruginosa** and is produced maximally during the late stationary phase of growth. Because PQS is an intercellular signal that is part of the quorum-sensing hierarchy and controls multiple virulence factors, basic studies designed to elucidate its biosynthetic pathway were begun. The data strongly suggest that anthranilate is a precursor for PQS. P. **aeruginosa** converted radiolabeled anthranilate into radioactive PQS, which was bioactive. An anthranilate analog (Me anthranilate) would **inhibit** the prodn. of PQS. This analog was then shown to have a major neg. effect on elastase prodn. by P. **aeruginosa** . These data provide evidence that precursors of intercellular

signals may provide viable targets for the development of therapeutic treatments that will reduce P. **aeruginosa** virulence.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:785293 HCAPLUS
DOCUMENT NUMBER: 134:291038
TITLE: The Pseudomonas **aeruginosa** lectins PA-IL and PA-IIL are controlled by quorum sensing and by RpoS
AUTHOR(S): Winzer, Klaus; Falconer, Colin; Garber, Nachman C.; Diggle, Stephen P.; Camara, Miguel; Williams, Paul
CORPORATE SOURCE: School of Pharmaceutical Sciences and Institute of Infections and Immunity, University of Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Journal of Bacteriology (2000), 182(22), 6401-6411
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In Pseudomonas **aeruginosa**, many exoproduct virulence determinants are regulated via a hierarchical quorum-sensing cascade involving the transcriptional regulators LasR and RhlR and their cognate activators, **N-(3-oxododecanoyl)-L-homoserine lactone (3O-C12-HSL)** and N-butanoyl-L-homoserine lactone (C4-HSL). In this paper, we demonstrate that the cytotoxic lectins PA-IL and PA-IIL are regulated via quorum sensing. Using immunoblot anal., the prodn. of both lectins was found to be directly dependent on the rhl locus while, in a lasR mutant, the onset of lectin synthesis was delayed but not abolished. The PA-IL structural gene, lecA, was cloned and sequenced. Transcript anal. indicated a monocistronic organization with a transcriptional start site 70 bp upstream of the lecA translational start codon. A lux box-type element together with RpoS (.sigma.S) consensus sequences was identified upstream of the putative promoter region. In Escherichia coli, expression of a lecA::lux reporter fusion was activated by RhlR/C4-HSL, but not by LasR/**3O-C12-HSL**, confirming direct regulation by RhlR/C4-HSL. Similarly, in P. **aeruginosa** PAO1, the expression of a chromosomal lecA::lux fusion was enhanced but not advanced by the addn. of exogenous C4-HSL but not **3O-C12-HSL**. Furthermore, mutation of rpoS abolished lectin synthesis in P. **aeruginosa**, demonstrating that both RpoS and RhlR/C4-HSL are required. Although the C4-HSL-dependent expression of the lecA::lux reporter in E. coli could be **inhibited** by the presence of **3O-C12-HSL**, this did not occur in P. **aeruginosa**. This suggests that, in the homologous genetic background, **3O-C12-HSL** does not function as a posttranslational regulator of the RhlR/C4-HSL-dependent activation of lecA expression.

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

Searcher : Shears 308-4994

IN THE RE FORMAT

L34 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:580652 HCAPLUS
DOCUMENT NUMBER: 131:319403
TITLE: Characterization of Pseudomonas **aeruginosa** enoyl-acyl carrier protein reductase (FabI): a target for the antimicrobial triclosan and its role in acylated homoserine lactone synthesis
AUTHOR(S): Hoang, Tung T.; Schweizer, Herbert P.
CORPORATE SOURCE: Department of Microbiology, Colorado State University, Fort Collins, CO, 80523, USA
SOURCE: Journal of Bacteriology (1999), 181(17), 5489-5497
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Pseudomonas **aeruginosa** fabI structural gene, encoding enoyl-acyl carrier protein (ACP) reductase, was cloned and sequenced. Nucleotide sequence anal. revealed that fabI is probably the last gene in a transcriptional unit that includes a gene encoding an ATP-binding protein of an ABC transporter of unknown function. The FabI protein was similar in size and primary sequence to other bacterial enoyl-ACP reductases, and it contained signature motifs for the FAD-dependent pyridine nucleotide reductase and glucose/ribitol dehydrogenase families, resp. The chromosomal fabI gene was disrupted, and the resulting mutant was viable but possessed only 62% of the total enoyl-ACP reductase activity found in wild-type cell exts. The fabI-encoded enoyl-ACP reductase activity was NADH dependent and **inhibited** by triclosan; the residual activity in the fabI mutant was also NADH dependent but not **inhibited** by triclosan. An polyhistidine-tagged FabI protein was purified and characterized. Purified FabI (i) could use NADH but not NADPH as a cofactor; (ii) used both crotonyl-CoA and crotonyl-ACP as substrates, although it was sixfold more active with crotonyl-ACP; and (iii) was efficiently **inhibited** by low concns. of triclosan. A FabI Gly95-to-Val active-site amino acid substitution was generated by site-directed mutagenesis, and the mutant protein was purified. The mutant FabI protein retained normal enoyl-ACP reductase activity but was highly triclosan resistant. When coupled to FabI, purified P. **aeruginosa** N-butyryl-L-homoserine lactone (C4-HSL) synthase, RhlI, could synthesize C4-HSL from crotonyl-ACP and S-adenosylmethionine. This reaction was NADH dependent and **inhibited** by triclosan. The levels of C4-HSL and **N-(3-oxo)-dodecanoyl**-L-homoserine **lactones** were reduced 50% in a fabI mutant, corroborating the role of FabI in acylated homoserine lactone synthesis in vivo.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 14:41:04 ON 22 NOV 2002)
L35 163 S L32
L36 37 S L35 AND INHIBIT?

Searcher : Shears 308-4994

L37 12 DUP REM L36 (25 DUPLICATES REMOVED)

L37 ANSWER 1 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 20023489[illegible] IN-PROCESS
DOCUMENT NUMBER: 22051038 PubMed ID: 12055291
TITLE: Lysophosphatidic acid **inhibition** of the accumulation of Pseudomonas **aeruginosa** PAO1 alginate, pyoverdin, elastase and LasA.
AUTHOR: Laux David C; Corson Joy M; Givskov Michael; Hentzer Morten; Moller Annette; Wosencroft Kathleen A; Olson Joan C; Krogfelt Karen A; Goldberg Joanna B; Cohen Paul S
CORPORATE SOURCE: Department of Cell and Molecular Biology, University of Rhode Island, Kingston, RI 02881, USA.
SOURCE: MICROBIOLOGY, (2002 Jun) 148 (Pt 6) 1709-23.
Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020703
Last Updated on STN: 20020703

AB The pathogenesis of Pseudomonas **aeruginosa** is at least partially attributable to its ability to synthesize and secrete the siderophore pyoverdin and the two zinc metalloproteases elastase and LasA, and its ability to form biofilms in which bacterial cells are embedded in an alginate matrix. In the present study, a lysophospholipid, 1-palmitoyl-2-hydroxy-sn-glycero-3-phosphate [also called monopalmitoylphosphatidic acid (MPPA)], which accumulates in inflammatory exudates, was shown to **inhibit** the extracellular accumulation of P. **aeruginosa** PAO1 alginate, elastase, LasA protease and the siderophore pyoverdin. MPPA also **inhibited** biofilm formation. The **inhibitory** effects of MPPA occur independently of rpoS expression and without affecting the accumulation of the autoinducers **N-(3-oxododecanoyl)** homoserine **lactone** and N-butyryl-L-homoserine lactone, and may be due, at least in part, to the ability of MPPA to bind divalent cations.

L37 ANSWER 2 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001525853 MEDLINE
DOCUMENT NUMBER: 21457347 PubMed ID: 11573001
TITLE: Interference with Pseudomonas quinolone signal synthesis **inhibits** virulence factor expression by Pseudomonas **aeruginosa**.
AUTHOR: Calfee M W; Coleman J P; Pesci E C
CORPORATE SOURCE: Department of Microbiology and Immunology, East Carolina University School of Medicine, 600 Moye Boulevard, Greenville, NC 27858, USA.
CONTRACT NUMBER: R01-AI46682 (NIAID)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Sep 25) 98 (20) 11633-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

Searcher : Shears 308-4994

ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010927
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Pseudomonas **aeruginosa** is an opportunistic pathogen that controls numerous virulence factors through intercellular signals. This bacterium has two quorum-sensing systems (las and rhl), which act through the intercellular signals **N-(3-oxododecanoyl)**-l-homoserine **lactone** (3-oxo-C(12)-HSL) and N-butyryl-l-homoserine lactone (C(4)-HSL), respectively. P. **aeruginosa** also produces a third intercellular signal that is involved in virulence factor regulation. This signal, 2-heptyl-3-hydroxy-4-quinolone [referred to as the Pseudomonas quinolone signal (PQS)], is a secondary metabolite that is part of the P. **aeruginosa** quorum-sensing hierarchy. PQS can induce both lasB (encodes LasB elastase) and rhlI (encodes the C(4)-HSL synthase) in P. **aeruginosa** and is produced maximally during the late stationary phase of growth. Because PQS is an intercellular signal that is part of the quorum-sensing hierarchy and controls multiple virulence factors, we began basic studies designed to elucidate its biosynthetic pathway. First, we present data that strongly suggest that anthranilate is a precursor for PQS. P. **aeruginosa** converted radiolabeled anthranilate into radioactive PQS, which was bioactive. We also found that an anthranilate analog (methyl anthranilate) would **inhibit** the production of PQS. This analog was then shown to have a major negative effect on elastase production by P. **aeruginosa**. These data provide evidence that precursors of intercellular signals may provide viable targets for the development of therapeutic treatments that will reduce P. **aeruginosa** virulence.

L37 ANSWER 3 OF 12 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:663190 SCISEARCH
THE GENUINE ARTICLE: 462PF
TITLE: Haemodynamic effects of the bacterial quorum sensing signal molecule, **N-(3-oxododecanoyl)**-L-homoserine **lactone**, in conscious, normal and endotoxaemic rats
AUTHOR: Gardiner S M (Reprint); Chhabra S R; Harty C; Williams P; Pritchard D I; Bycroft B W; Bennett T
CORPORATE SOURCE: Univ Nottingham, Sch Med, Queens Med Ctr, Sch Biomed Sci, Nottingham NG7 2RD, England (Reprint); Univ Nottingham, Queens Med Ctr, Inst Infect & Immun, Nottingham NG7 2RD, England; Univ Nottingham, Sch Pharmaceut Sci, Nottingham NG7 2RD, England
COUNTRY OF AUTHOR: England
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (AUG 2001) Vol. 133, No. 7, pp. 1047-1054.
Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 0007-1188.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB 1 N-acythomoserine lactones (AHLs) are small, diffusible signalling molecules, employed by Gramnegative bacteria to

coordinate gene expression with cell population density. Recent in vitro findings indicate that AHLs may function as virulence determinants per se, through modification of cytokine production by eukaryotic cells, and by stimulating the relaxation of blood vessels.

2 In the present study, we assessed the influence of AHLs on cardiovascular function in conscious rats, and draw attention to the ability of the **N-(3-oxododecanoyl)-L-homoserine lactone (3-oxo-C12-HSL)**, a signal molecule produced by P. **aeruginosa**, to cause marked bradycardia. This bradycardic effect was blocked by atropine and atenolol, and did not occur in vitro. Furthermore, modification of the acyl side chain length resulted in the loss of activity, whereas removal of the homoserine lactone ring, did not. The bradycardic effect of **3-oxo-C12-HSL** was also observed in endotoxaemic animals, albeit attenuated.

3 In normal rats, **3-oxo-C12-HSL** caused initial mesenteric and hindquarters vasoconstriction, but only slight, and delayed signs of vasodilatation in the renal and mesenteric vascular beds. Furthermore, administration of **3-oxo-C12-HSL** (pre-treatment or 2 h post-treatment) together with LPS, did not modify the established regional haemodynamic effects of the LPS, 6 It after the onset of its infusion.

4 Our observations do not provide any clear evidence for an ability of **3-oxo-C12-HSL** to modify the haemodynamic responses to LPS infusion. However, they are not inconsistent with the hypothesis that some of the cardiovascular sequelae of bacterial infection may be modulated by an influence of bacterial quorum sensing signalling molecules on the host.

L37 ANSWER 4 OF 12 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:778959 SCISEARCH
THE GENUINE ARTICLE: 475KK
TITLE: Can plants manipulate bacterial quorum sensing?
AUTHOR: Bauer W D (Reprint); Teplitski M
CORPORATE SOURCE: Ohio State Univ, Dept Hort & Crop Sci, 2021 Coffey Rd, Columbus, OH 43210 USA (Reprint); Ohio State Univ, Dept Hort & Crop Sci, Columbus, OH 43210 USA
COUNTRY OF AUTHOR: USA
SOURCE: AUSTRALIAN JOURNAL OF PLANT PHYSIOLOGY, (SEP 2001) Vol. 28, No. 9, pp. 913-921.
Publisher: C S I R O PUBLISHING, 150 OXFORD ST, PO BOX 1139, COLLINGWOOD, VICTORIA 3066, AUSTRALIA.
ISSN: 0310-7841.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 50

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Higher plants have been found to secrete a variety of unknown signal-mimic compounds that can stimulate or **inhibit** behaviors in bacteria, which are regulated by N-acyl homoserine lactone (AHL) signal molecules. A wide range of bacterial species use AHLs or other signal molecules to regulate the expression of many of their genes in response to changes in population density. Thus, the ability of higher plants to specifically alter AHL-regulated behavior in bacteria by production of AHL signal-mimic

compounds could be of broad consequence. We briefly review what is known about AHL signaling in bacteria and the synthesis of AHL signal-mimic compounds by plants, and then consider some of the important questions concerning the roles these plant signal-mimic compounds may play in natural encounters between plants and bacteria.

L37 ANSWER 5 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 3
ACCESSION NUMBER: 2000:542087 BIOSIS
DOCUMENT NUMBER: PREV200000542087
TITLE: Autoinducer molecule.
AUTHOR(S): Pearson, James P. (1); Gray, Kendall M.; Passador, Luciano; Tucker, Kenneth D.; Eberhard, Anatol; Iglewski, Barbara H.; Greenberg, Everett P.
CORPORATE SOURCE: (1) Iowa City, IA USA
ASSIGNEE: University of Iowa, Iowa City, IA, USA; University of Rochester; Ithaca College, Ithaca, NY, USA
PATENT INFORMATION: US 6057286 May 02, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 2, 2000) Vol. 1234, No. 1, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Autoinducer molecules, e.g., **N-(3-oxododecanoyl)**homoserine **lactone**, for Pseudomonas **aeruginosa** are described. The molecules regulate gene expression in the bacterium. Therapeutic compositions and therapeutic methods involving analogs and/or **inhibitors** of the autoinducer molecules also are described. The molecules are useful for treating or preventing infection by Pseudomonas **aeruginosa**.

L37 ANSWER 6 OF 12 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000507353 MEDLINE
DOCUMENT NUMBER: 20507809 PubMed ID: 11053384
TITLE: The Pseudomonas **aeruginosa** lectins PA-IL and PA-IIL are controlled by quorum sensing and by RpoS.
AUTHOR: Winzer K; Falconer C; Garber N C; Diggle S P; Camara M; Williams P
CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Nottingham, University Park, Nottingham NG7 2RD, United Kingdom.
SOURCE: JOURNAL OF BACTERIOLOGY, (2000 Nov) 182 (22) 6401-11.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF229814
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207
AB In Pseudomonas **aeruginosa**, many exoproduct virulence

Searcher : Shears 308-4994

determinants are regulated via a hierarchical quorum-sensing cascade involving the transcriptional regulators LasR and RhlR and their cognate activators, **N-(3-oxododecanoyl)-L-homoserine lactone (3O-C12-HSL)** and N-butanoyl-L-homoserine lactone (C4-HSL). In this paper, we demonstrate that the cytotoxic lectins PA-IL and PA-IIL are regulated via quorum sensing. Using immunoblot analysis, the production of both lectins was found to be directly dependent on the rhl locus while, in a lasR mutant, the onset of lectin synthesis was delayed but not abolished. The PA-IL structural gene, lecA, was cloned and sequenced. Transcript analysis indicated a monocistronic organization with a transcriptional start site 70 bp upstream of the lecA translational start codon. A lux box-type element together with RpoS (sigma(S)) consensus sequences was identified upstream of the putative promoter region. In Escherichia coli, expression of a lecA::lux reporter fusion was activated by RhlR/C4-HSL, but not by LasR/**3O-C12-HSL**, confirming direct regulation by RhlR/C4-HSL. Similarly, in P. **aeruginosa** PAO1, the expression of a chromosomal lecA::lux fusion was enhanced but not advanced by the addition of exogenous C4-HSL but not **3O-C12-HSL**. Furthermore, mutation of rpoS abolished lectin synthesis in P. **aeruginosa**, demonstrating that both RpoS and RhlR/C4-HSL are required. Although the C4-HSL-dependent expression of the lecA::lux reporter in E. coli could be **inhibited** by the presence of **3O-C12-HSL**, this did not occur in P. **aeruginosa**. This suggests that, in the homologous genetic background, **3O-C12-HSL** does not function as a posttranslational regulator of the RhlR/C4-HSL-dependent activation of lecA expression.

L37 ANSWER 7 OF 12 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999395061 MEDLINE
DOCUMENT NUMBER: 99395061 PubMed ID: 10464225
TITLE: Characterization of Pseudomonas **aeruginosa** enoyl-acyl carrier protein reductase (FabI): a target for the antimicrobial triclosan and its role in acylated homoserine lactone synthesis.
AUTHOR: Hoang T T; Schweizer H P
CORPORATE SOURCE: Department of Microbiology, Colorado State University, Fort Collins, Colorado 80523, USA.
CONTRACT NUMBER: GM56685 (NIGMS)
SOURCE: JOURNAL OF BACTERIOLOGY, (1999 Sep) 181 (17) 5489-97. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF104262
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991014
Last Updated on STN: 19991014
Entered Medline: 19991007

AB The Pseudomonas **aeruginosa** fabI structural gene, encoding enoyl-acyl carrier protein (ACP) reductase, was cloned and sequenced. Nucleotide sequence analysis revealed that fabI is probably the last gene in a transcriptional unit that includes a gene encoding an ATP-binding protein of an ABC transporter of

unknown function. The FabI protein was similar in size and primary sequence to other bacterial enoyl-ACP reductases, and it contained signature motifs for the FAD-dependent pyridine nucleotide reductase and glucose/ribitol dehydrogenase families, respectively. The chromosomal fabI gene was disrupted, and the resulting mutant was viable but possessed only 62% of the total enoyl-ACP reductase activity found in wild-type cell extracts. The fabI-encoded enoyl-ACP reductase activity was NADH dependent and **inhibited** by triclosan; the residual activity in the fabI mutant was also NADH dependent but not **inhibited** by triclosan. An polyhistidine-tagged FabI protein was purified and characterized. Purified FabI (i) could use NADH but not NADPH as a cofactor; (ii) used both crotonyl-coenzyme A and crotonyl-ACP as substrates, although it was sixfold more active with crotonyl-ACP; and (iii) was efficiently **inhibited** by low concentrations of triclosan. A FabI Gly95-to-Val active-site amino acid substitution was generated by site-directed mutagenesis, and the mutant protein was purified. The mutant FabI protein retained normal enoyl-ACP reductase activity but was highly triclosan resistant. When coupled to FabI, purified P. **aeruginosa** N-butyryl-L-homoserine lactone (C4-HSL) synthase, RhlI, could synthesize C4-HSL from crotonyl-ACP and S-adenosylmethionine. This reaction was NADH dependent and **inhibited** by triclosan. The levels of C4-HSL and **N-(3-oxo)-dodecanoyl**-L-homoserine **lactones** were reduced 50% in a fabI mutant, corroborating the role of FabI in acylated homoserine lactone synthesis in vivo.

L37 ANSWER 8 OF 12 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999426798 MEDLINE
DOCUMENT NUMBER: 99426798 PubMed ID: 10496880
TITLE: Pseudomonas **aeruginosa** quorum-sensing signal molecule **N-(3-oxododecanoyl)**-L-homoserine **lactone inhibits** expression of P2Y receptors in cystic fibrosis tracheal gland cells.
AUTHOR: Saleh A; Figarella C; Kammouni W; Marchand-Pinatel S; Lazdunski A; Tubul A; Brun P; Merten M D
CORPORATE SOURCE: Groupe de Recherche sur les Glandes Exocrines, Faculte de Medecine, 13385 Marseille 05, France.
SOURCE: INFECTION AND IMMUNITY, (1999 Oct) 67 (10) 5076-82. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991014

AB ATP and UTP have been proposed for use as therapeutic treatment of the abnormal ion transport in the airway epithelium in cystic fibrosis (CF), the most characteristic feature of which is permanent infection by Pseudomonas **aeruginosa**. As for diverse gram-negative bacteria, this pathogenic bacterium accumulates diffusible N-acylhomoserine lactone (AHL) signal molecules, and when a threshold concentration is reached, virulence factor genes are activated. Human submucosal tracheal gland serous (HTGS) cells are

believed to play a major role in the physiopathology of CF. Since ATP and UTP stimulate CF epithelial cells through P2Y receptors, we sought to determine whether CF HTGS cells are capable of responding to the AHLs N-butanoyl-L-homoserine lactone (BHL), N-hexanoyl-L-homoserine lactone (HHL), **N-(3-oxododecanoyl)-L-homoserine lactone** (OdDHL), and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL), with special reference to P2Y receptors. All AHLs **inhibited** ATP- and UTP-induced secretion by CF HTGS cells. The 50% **inhibitory** concentrations were as high as 10 and 5 &mgr;M for BHL and HHL, respectively, but were only 0.3 and 0.4 pM for OdDHL and OHHL, respectively. Furthermore, all AHLs down-regulated the expression of the P2Y2 and P2Y4 receptors. Ibuprofen and nordihydroguaiaretic acid were able to prevent AHL **inhibition** of the responses to nucleotides, but neither dexamethasone nor indomethacin was able to do this. These data indicate that AHLs may alter responsiveness to ATP and UTP by CF HTGS cells and suggest that, in addition to ATP and/or UTP analogues, ibuprofen may be of use for a combinational pharmacological therapy for CF.

L37 ANSWER 9 OF 12 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999138741 MEDLINE
DOCUMENT NUMBER: 99138741 PubMed ID: 9973347
TITLE: Active efflux and diffusion are involved in transport of Pseudomonas **aeruginosa** cell-to-cell signals.
AUTHOR: Pearson J P; Van Delden C; Iglewski B H
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester, Rochester, New York 14642, USA.
CONTRACT NUMBER: 5T32AI07362 (NIAID)
AI33713 (NIAID)
SOURCE: JOURNAL OF BACTERIOLOGY, (1999 Feb) 181 (4) 1203-10.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990402
Last Updated on STN: 19990402
Entered Medline: 19990322

AB Many gram-negative bacteria communicate by N-acyl homoserine lactone signals called autoinducers (AIs). In Pseudomonas **aeruginosa**, cell-to-cell signaling controls expression of extracellular virulence factors, the type II secretion apparatus, a stationary-phase sigma factor (sigmas), and biofilm differentiation. The fact that a similar signal, N-(3-oxohexanoyl) homoserine lactone, freely diffuses through Vibrio fischeri and Escherichia coli cells has led to the assumption that all AIs are freely diffusible. In this work, transport of the two P. **aeruginosa** AIs, **N-(3-oxododecanoyl)** homoserine **lactone** (3OC12-HSL) (formerly called PAI-1) and N-butyryl homoserine lactone (C4-HSL) (formerly called PAI-2), was studied by using tritium-labeled signals. When [3H]C4-HSL was added to cell suspensions of P. **aeruginosa**, the cellular concentration reached a steady state in less than 30 s and was nearly equal to the external concentration, as expected for a freely diffusible compound. In contrast, [3H]3OC12-HSL required about 5 min to reach a

steady state, and the cellular concentration was 3 times higher than the external level. Addition of **inhibitors** of the cytoplasmic membrane proton gradient, such as azide, led to a strong increase in cellular accumulation of [3H]3OC12-HSL, suggesting the involvement of active efflux. A defined mutant lacking the mexA-mexB-oprM-encoded active-efflux pump accumulated [3H]3OC12-HSL to levels similar to those in the azide-treated wild-type cells. Efflux experiments confirmed these observations. Our results show that in contrast to the case for C4-HSL, P. **aeruginosa** cells are not freely permeable to 3OC12-HSL. Instead, the mexA-mexB-oprM-encoded efflux pump is involved in active efflux of 3OC12-HSL. Apparently the length and/or degree of substitution of the N-acyl side chain determines whether an AI is freely diffusible or is subject to active efflux by P. **aeruginosa**.

L37 ANSWER 10 OF 12 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2000025555 MEDLINE
DOCUMENT NUMBER: 20025555 PubMed ID: 10556916
TITLE: The Pseudomonas **aeruginosa** quorum-sensing signal molecule, **N-(3-oxododecanoyl)**-L-homoserine **lactone**, **inhibits** porcine arterial smooth muscle contraction.
AUTHOR: Lawrence R N; Dunn W R; Bycroft B; Camara M; Chhabra S R; Williams P; Wilson V G
CORPORATE SOURCE: School of Biomedical Sciences, The Queen's Medical Centre, Clifton Boulevard, Nottingham, NG7 2UH, UK.
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1999 Oct) 128 (4) 845-8.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000606
Entered Medline: 19991214

AB The Pseudomonas **aeruginosa** quorum sensing molecule **N-(3-oxododecanoyl)**-L-homoserine **lactone** (OdDHL) has been shown to suppress cytokine production in macrophages. We have examined the effect of OdDHL and related compounds on constrictor tone of porcine blood vessels. OdDHL (1-30 microM) caused a concentration-dependent **inhibition** of U46619-induced contractions of the coronary artery through a largely endothelium-independent mechanism, but was markedly less effective in the pulmonary artery. Quantitively similar effects to those produced by OdDHL were observed with N-(3-oxododecanoyl)-L-homocysteine thiolactone, a thiolactone derivative, while N-3-oxododecanamide, a lactone-free acyl analogue, possessed 1/3rd the potency as a vasorelaxant. Neither N-butanoyl-L-homoserine lactone nor L-homoserine lactone (up to 30 microM) were active. Our findings indicate that OdDHL **inhibits** vasoconstrictor tone of both pulmonary and coronary blood vessels from the pig. The vasorelaxant action of OdDHL appears to be primarily determined by the N-acyl chain length, with a minor contribution by the homoserine lactone moiety.

Searcher : Shears 308-4994

L37 ANSWER 11 OF 12 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998084452 MEDLINE
DOCUMENT NUMBER: 98084452 PubMed ID: 9423836
TITLE: The Pseudomonas **aeruginosa** quorum-sensing signal molecule **N-(3-oxododecanoyl)**-L-homoserine **lactone** has immunomodulatory activity.
AUTHOR: Telford G; Wheeler D; Williams P; Tomkins P T; Appleby P; Sewell H; Stewart G S; Bycroft B W; Pritchard D I
CORPORATE SOURCE: Department of Life Science, University of Nottingham, University Park, United Kingdom.
SOURCE: INFECTION AND IMMUNITY, (1998 Jan) 66 (1) 36-42. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980127

AB Diverse gram-negative bacterial cells communicate with each other by using diffusible N-acyl homoserine lactone (AHL) signal molecules to coordinate gene expression with cell population density. Accumulation of AHLs above a threshold concentration renders the population "quorate," and the appropriate target gene is activated. In pathogenic bacteria, such as Pseudomonas **aeruginosa**, AHL-mediated quorum sensing is involved in the regulation of multiple virulence determinants. We therefore sought to determine whether the immune system is capable of responding to these bacterial signal molecules. Consequently the immunomodulatory properties of the AHLs **N-(3-oxododecanoyl)**-L-homoserine **lactone** (OdDHL) and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL) were evaluated in murine and human leukocyte immunoassays in vitro. OdDHL, but not OHHL, **inhibited** lymphocyte proliferation and tumor necrosis factor alpha production by lipopolysaccharide-stimulated macrophages. Furthermore, OdDHL simultaneously and potently down-regulated the production of IL-12, a Th-1-supportive cytokine. At high concentrations (>7 x 10(-5) M) OdDHL **inhibited** antibody production by keyhole limpet hemocyanin-stimulated spleen cells, but at lower concentrations (<7 x 10(-5) M), antibody production was stimulated, apparently by increasing the proportion of the immunoglobulin G1 (IgG1) isotype. OdDHL also promoted IgE production by interleukin-4-stimulated human peripheral blood mononuclear cells. These data indicate that OdDHL may influence the Th-1-Th-2 balance in the infected host and suggest that, in addition to regulating the expression of virulence determinants, OdDHL may contribute to the pathogenesis of P. **aeruginosa** infections by functioning as a virulence determinant per se.

L37 ANSWER 12 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-098943 [09] WPIDS
CROSS REFERENCE: 2000-339615 [29]
DOC. NO. CPI: C1997-031582
TITLE: New auto-inducer(s), e.g. **N-(3-oxo-dodecanoyl)** homoserine

Searcher : Shears 308-4994

lactone - used to **inhibit** infectivity of Pseudomonas **aeruginosa** and to treat immuno-compromised individuals infected with P. **aeruginosa**.

DERWENT CLASS: B03
INVENTOR(S): EBERHARD, A; GRAY, K M; GREENBERG, E P; IGLEWSKI, B H; PASSADOR, L; PEARSON, J P; TUCKER, K D
PATENT ASSIGNEE(S): (ITHA-N) ITHACA COLLEGE; (IOWA) UNIV IOWA RES FOUND; (UYRP) UNIV ROCHESTER
COUNTRY COUNT: 1
PATENT INFORMATION:

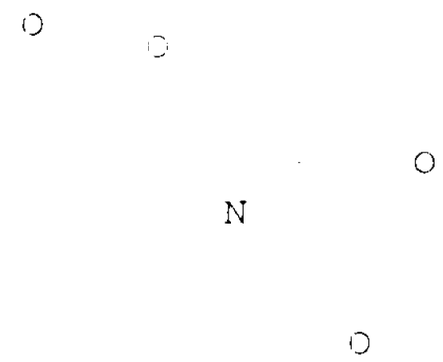
PATENT NO	KIND	DATE	WEEK	LA	PG
US 5591872	A	19970107	(199709)*		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5591872	A	US 1993-104487	19930809

PRIORITY APPLN. INFO: US 1993-104487 19930809
AN 1997-098943 [09] WPIDS
CR 2000-338615 [29]
AB US 5591872 A UPAB: 20000617
Autoinducer molecules of formula (I), which are able to regulate gene expression, are new. X = O, S or NH; Y = O; and Z1, Z2 = H, O, S or NH.
USE - (I) **inhibit** the activity of the Las R protein of Pseudomonas **aeruginosa** and/or **inhibit** the autoinducer activity of **N**-(**3-oxododecanoyl**) homoserine **lactone** and a carrier.
The cpds. can also be used to **inhibit** the infectivity of P. **aeruginosa** and to treat an immunocompromised individual infected with P. **aeruginosa**.
Dwg.0/4

FILE 'HOME' ENTERED AT 14:42:19 ON 22 NOV 2002



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=> s l5 and 3-oxododecanoyl

        4219014 3
             34 OXODODECANOYL
             29 3-OXODODECANOYL
                (3(W)OXODODECANOYL)
L7           21 L5 AND 3-OXODODECANOYL

=> d l7 1-21 ibib abs hitstr
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L7 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:150310 CAPLUS
DOCUMENT NUMBER: 132:179668
TITLE: Production enhancement of antibiotic with Pseudomonas
INVENTOR(S): Nakata, Kunio
PATENT ASSIGNEE(S): Tsusho Sangyosho Kiso Sangyo Kyoku, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

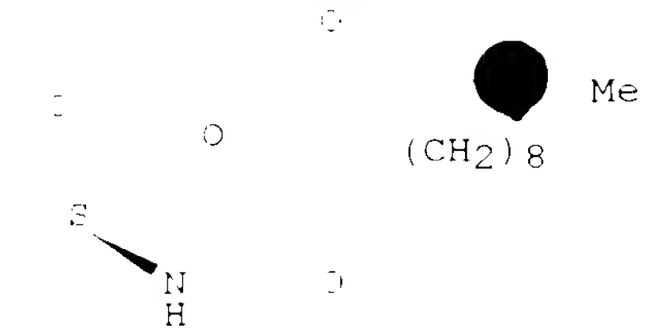
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000069985	A2	20000307	JP 1998-261026	19980901

AB Prodn. of agrochem. antibiotics pyoluteorin, 2,4-diacetylphloroglucinol, and N-(**3-oxododecanoyl**)-L-homoserine lactone with P. fluorescens is enhanced by application of stress condition to the microorganism in the process of culturing. The stress condition is selected from excess ethanol, excess salt, and elevated temp.

IT **168982-69-2P**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(prodn. enhancement of antibiotic with Pseudomonas)

RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



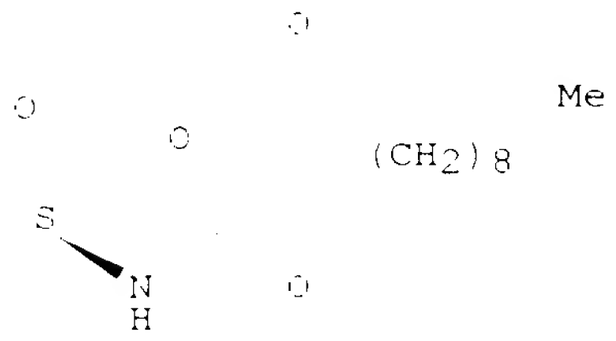
L7 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:767972 CAPLUS
DOCUMENT NUMBER: 132:103570
TITLE: Identification of genes controlled by quorum sensing in Pseudomonas aeruginosa
AUTHOR(S): Whiteley, Marvin; Lee, Kimberly M.; Greenberg, E. P.
CORPORATE SOURCE: Department of Microbiology, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(24), 13904-13909
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacteria communicate with each other to coordinate expression of specific genes in a cell d.-dependent fashion, a phenomenon called quorum sensing and response. Although we know that quorum sensing via acyl-homoserine lactone (HSL) signals controls expression of several virulence genes in the human pathogen Pseudomonas aeruginosa, the no. and types of genes controlled by quorum sensing have not been studied systematically. We have constructed a library of random insertions in the chromosome of a P. aeruginosa acyl-HSL synthesis mutant by using a transposon contg. a promoterless lacZ. This library was screened for acyl-HSL induction of lacZ. Thirty-nine quorum sensing-regulated genes were identified. The genes were organized into classes depending on the pattern of regulation. About half of the genes appear to be in seven operons, some seem organized in large patches on the genome. Many of the quorum sensing-regulated genes code for putative virulence factors or prodn. of secondary metabolites. Many of the genes identified showed a high level of induction by acyl-HSL signaling.

IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(identification, characterization and chromosome mapping of genes controlled by quorum sensing in Pseudomonas aeruginosa, high level of induction by acyl-HSL signaling)

RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48
REFERENCE(S): (2) Berg, D; Genetics 1983, V105, P813 CAPLUS
(3) Brint, J; J Bacteriol 1[illegible], V177, P7155 CAPLUS
(5) Chapon-Herve, V; Mol Microbiol 1997, V24, P1169 CAPLUS
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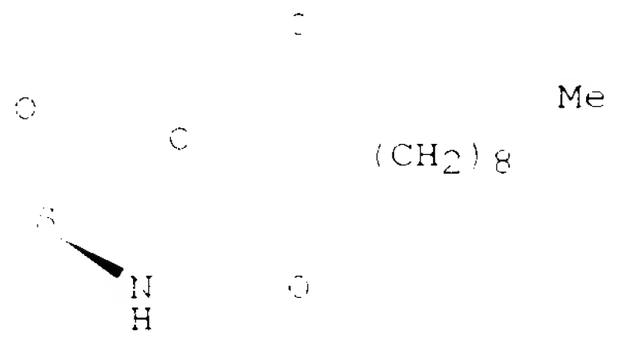
(7) Davies, D; Science 1998, V280, P295 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:714186 CAPLUS
DOCUMENT NUMBER: 132:30331
TITLE: The Pseudomonas aeruginosa quorum-sensing signal molecule, N-(**3-oxododecanoyl**)-L-homoserine lactone, inhibits porcine arterial smooth muscle contraction
AUTHOR(S): Lawrence, R. N.; Dunn, W. R.; Bycroft, B.; Camara, M.; Chhabra, S. R.; Williams, P.; Wilson, V. G.
CORPORATE SOURCE: School of Biomedical Sciences, The Queen's Medical Centre, Nottingham, NG7 2UH, UK
SOURCE: Br. J. Pharmacol. (1999), 128(4), 845-848
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Pseudomonas aeruginosa quorum sensing mol. N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL) has been shown to suppress cytokine prodn. in macrophages. We have examd. the effect of OdDHL and related compds. on constrictor tone of porcine blood vessels. OdDHL (1-30 .mu.M) caused a concn.-dependent inhibition of U46619-induced contractions of the coronary artery through a largely endothelium-independent mechanism, but was markedly less effective in the pulmonary artery. Quant. similar effects to those produced by OdDHL were obsd. with N-(**3-oxododecanoyl**)-L-homocysteine thiolactone, a thiolactone deriv., while N-3-oxododecanamide, a lactone-free acyl analog, possessed 1/3rd the potency as a vasorelaxant. Neither N-butanoyl-L-homoserine lactone nor L-homoserine lactone (up to 30 .mu.M) were active. Our findings indicate that OdDHL inhibits vasoconstrictor tone of both pulmonary and coronary blood vessels from the pig. The vasorelaxant action of OdDHL appears to be primarily detd. by the N-acyl chain length, with a minor contribution by the homoserine lactone moiety.
IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vasodilating effects of (oxododecanoyl)homoserine lactone and analogs on porcine arterial smooth muscle contraction)
RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17
REFERENCE(S):
(1) Bainton, N; Gene 1992, V116, P87 CAPLUS
(2) Chhabra, S; J Antibiotics 1993, V46, P441 CAPLUS
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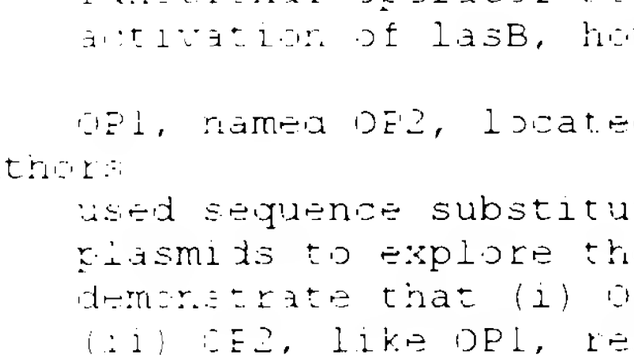
(5) Finch, R; J Antimicrobial Chemotherapy 1998, V42, P569 CAPLUS
(7) Henderson, B; Cytokine 1996, V8, P264 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

17 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:681880 CAPLUS
DOCUMENT NUMBER: 132:31556
TITLE: A second operator is involved in Pseudomonas aeruginosa elastase (lasB) activation
AUTHOR(S): Anderson, Ronda M.; Zimprich, Chad A.; Rust, Lynn
CORPORATE SOURCE: Department of Veterinary and Microbiological Sciences, North Dakota State University, Fargo, ND, 58105, USA
SOURCE: J. Bacteriol. (1999), 181(20), 6264-6270
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pseudomonas aeruginosa LasB elastase gene (lasB) transcription is controlled by the two-component quorum-sensing system of LasR, and the autoinducer, 3OC12-HSL (N-**3**-[**oxododecanoyl**]homoserine lactone). LasR and 3OC12-HSL-mediated lasB activation requires a functional operator sequence (OP1) in the lasB promoter region. Optimal activation of lasB, however, requires a second sequence of 76 identity to OP1, named OP2, located 43 bp upstream of OP1. In this study, the authors used sequence substitutions and insertion mutations in lasBp-lacZ fusion plasmids to explore the role of OP2 in lasB activation. These results demonstrate that (i) OP1 and OP2 synergistically mediate lasB activation; (ii) OP2, like OP1, responds to LasR and 3OC12-HSL; and (iii) the putative autoinducer-binding domain of LasR is not required for synergistic activation from OP1 and OP2.
IT **168982-69-2**, N-**3**-[**Oxododecanoyl**]homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(3OC12-HSL regulating OP2 and OP1; second operator is involved in Pseudomonas aeruginosa elastase (lasB) activation)
RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50
REFERENCE(S):
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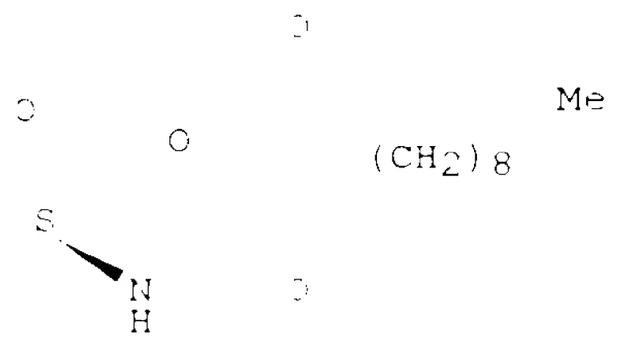
(4) Berg, O; Biochemistry 1981, V20, P6929 CAPLUS
(5) Bever, R; J Bacteriol 1988, V170, P4309 CAPLUS
(6) Bingham, A; Gene 1986, [illegible], P67 CAPLUS
(7) Brint, J; J Bacteriol 1995, V177, P7155 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:651479 CAPLUS
DOCUMENT NUMBER: 132:10592
TITLE: Quorum sensing-dependent regulation and blockade of exoprotease production in Aeromonas hydrophila
AUTHOR(S): Swift, Simon; Lynch, Martin J.; Fish, Leigh; Kirke, David F.; Tomas, Juan M.; Stewart, Gordon S. A. B.; Williams, Paul
CORPORATE SOURCE: Institute of Infections and Immunity, Queen's Medical Centre, University of Nottingham, Nottingham, NG7 2UH, UK
SOURCE: Infect. Immun. (1999), 67(10), 5192-5199
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Aeromonas hydrophila, the ahyI gene encodes a protein responsible for the synthesis of the quorum sensing signal N-butanoyl-L-homoserine lactone (C4-HSL). Inactivation of the ahyI gene on the A. hydrophila chromosome abolishes C4-HSL prodn. The exoprotease activity of A. hydrophila consists of both serine protease and metalloprotease activities; in the ahyI-neg. strain, both are substantially reduced but can be restored by the addn. of exogenous C4-HSL. In contrast, mutation of the LuxR homolog AhyR results in the loss of both exoprotease activities, which cannot be restored by exogenous C4-HSL. Furthermore, a substantial redn. in the prodn. of exoprotease by the ahyI+ parent strain is obtained by the addn. of N-acylhomoserine lactone analogs that have acyl side chains of 10, 12, or 14 carbons. The inclusion of N-(**3-oxododecanoyl**)-L-homoserine lactone or N-(3-oxotetradecanoyl)-L-homoserine lactone at 10 .mu.M in overnight cultures of A. hydrophila abolishes exoprotease prodn. in azocasein assays and reduces the activity of all the exoprotease species seen in zymograms.
IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(quorum sensing-dependent regulation and blockade of exoprotease prodn. in Aeromonas hydrophila)
RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 65
REFERENCE(S): (2) Chapon-Herve, V; Mol Microbiol 1997, V24, P1169

CAPLUS
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(4) Coleman, G; Biochem Soc Trans 1993, V21, P49S CAPLUS
(5) Cai, Y; J Bacteriol 1995, V177, P5108 CAPLUS
(6) Denis, F; Can J Microbiol 1984, V30, P1190 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

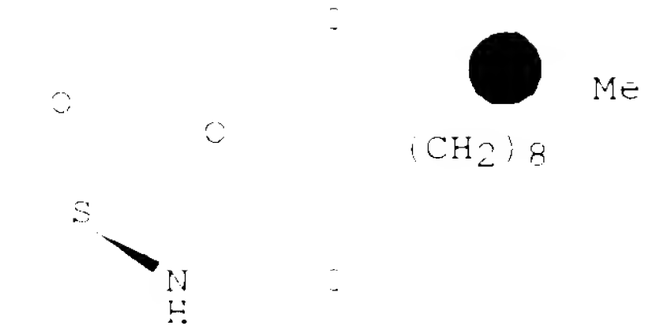
L7 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:651464 CAPLUS
DOCUMENT NUMBER: 132:376
TITLE: Pseudomonas aeruginosa quorum-sensing signal molecule N-(**3-oxododecanoyl**)-L-homoserine lactone inhibits expression of P2Y receptors in cystic fibrosis tracheal gland cells
AUTHOR(S): Saleh, A.; Figarella, C.; Kammouni, W.; Marchand-Pinatel, S.; Lazdunski, A.; Tubul, A.; Brun, P.; Merten, M. D.
CORPORATE SOURCE: Groupe de Recherche sur les Glandes Exocrines, Faculte de Medecine, Marseille, 13385/09, Fr.
SOURCE: Infect. Immun. (1999), 67(10), 5076-5082
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ATP and UTP have been proposed for use as therapeutic treatment of the abnormal ion transport in the airway epithelium in cystic fibrosis (CF), the most characteristic feature of which is permanent infection by Pseudomonas aeruginosa. As for diverse gram-neg. bacteria, this pathogenic bacterium accumulates diffusible N-acylhomoserine lactone (AHL) signal mols., and when a threshold concn. is reached, virulence factor genes are activated. Human submucosal tracheal gland serous (HTGS) cells are believed to play a major role in the physiopathol. of CF. Since ATP and UTP stimulate CF epithelial cells through P2Y receptors, we sought to det. whether CF HTGS cells are capable of responding to the AHLs N-butanoyl-L-homoserine lactone (BHL), N-hexanoyl-L-homoserine lactone (HHL), N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL), and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL), with special ref. to P2Y receptors. All AHLs inhibited ATP- and UTP-induced secretion by CF HTGS cells. The 50% inhibitory concns. were as high as 10 and 5 .mu.M for BHL and HHL, resp., but were only 0.3 and 0.4 pM for OdDHL and OHHL, resp. Furthermore, all AHLs down-regulated the expression of the P2Y2 and P2Y4 receptors. Ibuprofen and nordihydroguaiaretic acid were able to prevent AHL inhibition of the responses to nucleotides, but neither dexamethasone nor indomethacin was able to do this. These data indicate that AHLs may alter responsiveness to ATP and UTP by CF HTGS cells and suggest that, in addn. to ATP and/or UTP analogs, ibuprofen may be of use for a combinational pharmacol. therapy for CF.

IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(Pseudomonas aeruginosa quorum-sensing N-acylhomoserine lactone signal mols. inhibit expression of P2Y receptors in cystic fibrosis tracheal gland cells and effects of ATP-UTP and ibuprofen)

RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49
REFERENCE(S):
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(6) Brennan, P; Biochem Pharmacol 1994, V55, P965 CAPLUS
(7) Bryan, R; Am J Respir Cell Mol Biol 1998, V19, P269 CAPLUS
(8) Chhabra, S; Antibiotics (Tokyo) 1993, V46, P441 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:472029 CAPLUS
DOCUMENT NUMBER: 131:27946
TITLE: Homoserine lactone derivatives as antibacterial agents
and for control of biofilm formation
INVENTOR(S): Rycroft, Barrie Walsham; Fish, Leigh; Hope, Victoria Jane; Lynch, Martin John; Milton, Debra Lynn; Swift, Simon; Stewart, Gordon Sydney Anderson Birnie; Williams, Paul
PATENT ASSIGNEE(S): The University of Nottingham, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9927746	A1	19990610	WO 1998-GB3548	19981126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9912524	A1	19990616	AU 1999-12524	19981126
PRIORITY APPLN. INFO.:			GB 1997-25599	19971204
			WO 1998-GB3548	19981126

OTHER SOURCE(S): MARPAT 131:27946
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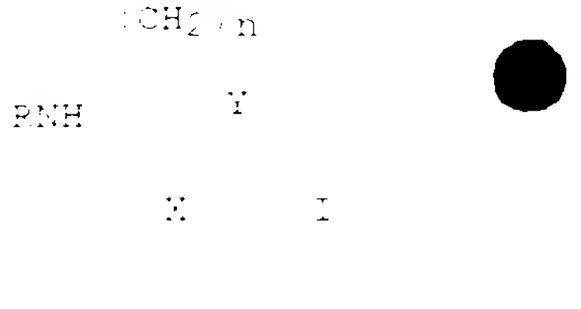


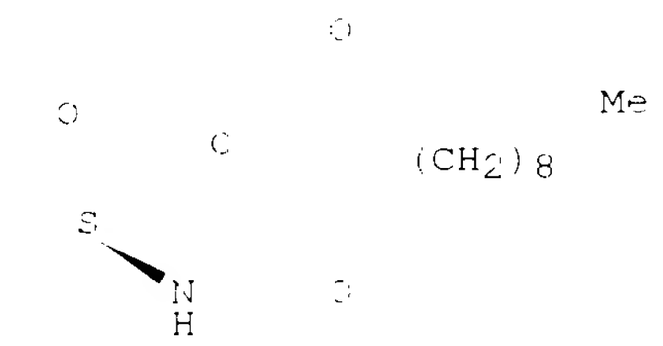
AB Compds. I [n = 2, 3; X, Y = O, S, NH; R = (un)substituted C1-C18 alkyl or acyl] may be used in the treatment or prevention of a bacterial infection in humans or animals by control of colonization. The compds. may also be employed to remove biofilms from surfaces and are therefore useful in antibacterial articles and compns.

IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homoserine lactone derivs. as antibacterial agents and for control of biofilm formation)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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REFERENCE(S): (1) Allison, D; FEMS Microbiol Lett 1998, V167(2), P179 CAPLUS
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(5) Givskov, M; J Bacteriol 1996, V178(22), P6618 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:169359 CAPLUS
DOCUMENT NUMBER: 130:279069
TITLE: Promotion of antibiotic production by high ethanol, high NaCl concentration, or heat shock in Pseudomonas fluorescens S272
AUTHOR(S): Nakata, Kuniho; Yoshimoto, Akihiro; Yamada, Yasuhiro
CORPORATE SOURCE: Central Research Laboratories, Meiji Seika Corporation, Fujisawa, 251-0057, Japan
SOURCE: Biosci., Biotechnol., Biochem. (1999), 63(2), 293-297
CODEN: BBBIEJ; ISSN: 0916-8451
PUBLISHER: Japan Society for Bioscience, Biotechnology, and Agrochemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A stress imposed by a continuous feed of high ethanol, high NaCl concn., or a high temp. shock increased antibiotic prodn. by several times in Pseudomonas fluorescens S272. A tentative bioassay showed that the stress caused about 40-fold elevation in the autoinducer activity. Addn. of

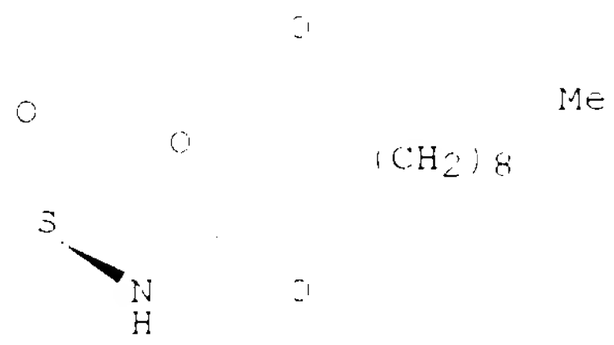
synthetic autoinducers, N-(**3-oxododecanoyl**
-L-homoserine lactone or N-(3-oxohexanoyl)-L-homoserine lactone at a
concn. of more than 100 .mu.g/L to a non-stressed culture also increased
the antibiotic prodn. by several times. These results suggested that
antibiotic prodn. in P. fluorescens S272 was regulated by
N-acyl-homoserine lactone and that the promotive effect by stress
occurred
through any function that increased the autoinducer prodn.

IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine
lactone
RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(in promotion of antibiotic formation by Pseudomonas fluorescens)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



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CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2006 ACS
ACCESSION NUMBER: 1999:149906 CAPLUS
DOCUMENT NUMBER: 130:293770
TITLE: Active efflux and diffusion are involved in transport
of Pseudomonas aeruginosa cell-to-cell signals
AUTHOR(S): Pearson, James P.; Van Delden, Christian; Iglewski,
Barbara H.
CORPORATE SOURCE: Department of Microbiology and Immunology, University
of Rochester, Rochester, NY, 14642, USA
SOURCE: J. Bacteriol. (1999), 181(4), 1203-1210
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

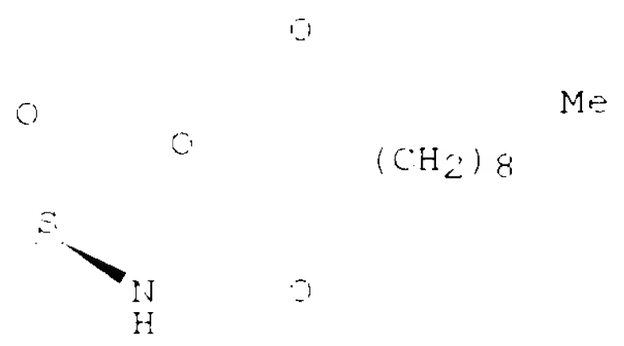
AB Many gram-neg. bacteria communicate by N-acyl homoserine lactone signals
called autoinducers (AIs). In Pseudomonas aeruginosa, cell-to-cell
signaling controls expression of extracellular virulence factors, the
type
II secretion app., a stationary-phase sigma factor (.sigma.S), and
biofilm
differentiation. The fact that a similar signal, N-(3-oxohexanoyl)
homoserine lactone, freely diffuses through Vibrio fischeri and
Escherichia coli cells has led to the assumption that all AIs are freely
diffusible. In this work, transport of the two P. aeruginosa AIs, N-(
3-oxododecanoyl) homoserine lactone (3OC12-HSL)
(formerly called PAI-1) and N-butyryl homoserine lactone (C4-HSL)
(formerly called PAI-2), was studied by using tritium-labeled signals.

When [3H]C4-HSL was added to cell suspensions of P. aeruginosa, the cellular concn. reached a steady state in less than 30 s and was nearly equal to the external concn., as expected for a freely diffusible compd. In contrast, [3H]3OC12-HSL required about 5 min to reach a steady state, and the cellular concn. was 3 times higher than the external level. Addn. of inhibitors of the cytoplasmic membrane proton gradient, such as azide, led to a strong increase in cellular accumulation of [3H]3OC12-HSL, suggesting the involvement of active efflux. A defined mutant lacking the mexA-mexB-oprM-encoded active-efflux pump accumulated [3H]3OC12-HSL to levels similar to those in the azide-treated wild-type cells. Efflux expts. confirmed these observations. Our results show that in contrast to the case for C4-HSL, P. aeruginosa cells are not freely permeable to 3OC12-HSL. Instead, the mexA-mexB-oprM-encoded efflux pump is involved in active efflux of 3OC12-HSL. Apparently the length and/or degree of substitution of the N-acyl side chain dets. whether an AI is freely diffusible or is subject to active efflux by P. aeruginosa.

IT **168982-69-2**, N-(**3-Oxododecanoyl**) homoserine lactone
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(autoinducer; active efflux and diffusion are involved in transport of Pseudomonas aeruginosa cell-to-cell signals)

RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42
REFERENCE(S):
(1) Brint, J; J Bacteriol 1995, V177, P7155 CAPLUS
(2) Burns, J; Antimicrob Agents Chemother 1996, V40, P307 CAPLUS
(3) Chapon-Herve, V; Mol Microbiol 1997, V24, P1169 CAPLUS
(4) Davies, D; Science 1998, V280, P295 CAPLUS
(6) Evans, K; J Bacteriol 1998, V180, P5443 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:116007 CAPLUS
DOCUMENT NUMBER: 130:222191
TITLE: Correlation between autoinducers and rhamnolipids production by Pseudomonas aeruginosa IFO 3924
AUTHOR(S): Nakata, Kuniho; Yoshimoto, Akihiro; Yamada, Yasuhiro
CORPORATE SOURCE: Central Research Laboratories, Meiji Seika Corporation, Fujisawa, 251-0057, Japan
SOURCE: J. Ferment. Bioeng. (1998), 86(6), 608-610
CODEN: JFBIEX; ISSN: 0922-338X
PUBLISHER: Society for Fermentation and Bioengineering, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB High rhamnolipid productivity (32 g/l) was obtained in an ethanol

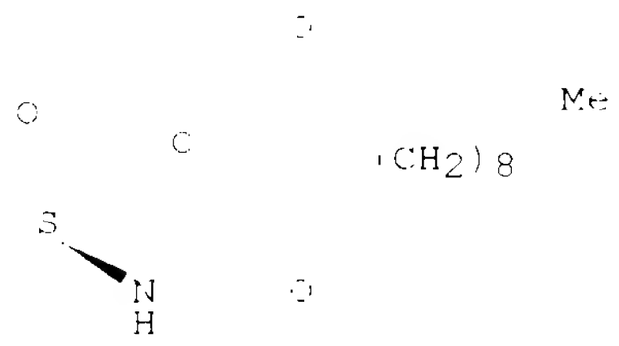
fed-batch culture of Pseudomonas aeruginosa IFO 3924. Examn. of the autoinducer level and exogenous autoinducer addn. tests indicated that in the fed-batch system high autoinducer activity, which was about ten-fold that obtained in an unfed system, was thought to be the cause of the high rate of rhamnolipid prodn. Both N-(3-oxohexanoyl)-L-homoserine lactone (OHHL) and N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL) enhanced rhamnolipid productivity in the unfed system.

IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(correlation between autoinducers and rhamnolipids prodn. by Pseudomonas aeruginosa IFO 3924)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5
REFERENCE(S):
(1) Matsufuji, M; Biotechnol Lett 1997, V19, P1213 CAPLUS
(2) Ochsner, U; J Bacteriol 1994, V176, P2044 CAPLUS
(3) Osman, M; J Am Oil Chem Soc 1996, V73, P851 CAPLUS
(4) Pearson, J; Proc Natl Acad Sci USA 1994, V91, P197 CAPLUS
(5) Shaw, P; Proc Natl Acad Sci USA 1997, V94, P6036 CAPLUS

L7 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:9682 CAPLUS
DOCUMENT NUMBER: 130:68217
TITLE: Methods and compositions for controlling biofilm development
INVENTOR(S): Davies, David G.; Costerton, John William
PATENT ASSIGNEE(S): The Research and Development Institute, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9857761-	A1	19981223	WO 1998-US12695	19980618
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 9858075	A2	19981223	WO 1998-US12728	19980617
WO 9858075	A3	19990318		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

AU 9882589 A1 19990104 AU 1998-82589 19980617
EP 994961 A2 20000426 EP 1998-[redacted]782 19980617
R: AT, BE, [redacted]H, DE, DK, ES, FR, GB, GR, IT, [redacted]I, LU, NL, SE, MC, PT, IE, FI
AU 9879776 A1 19990104 AU 1998-79776 19980618
PRIORITY APPLN. INFO.: US 1997-50093 19970618
WO 1998-US12728 19980617
WO 1998-US12695 19980618

OTHER SOURCE(S): MARPAT 129:68217

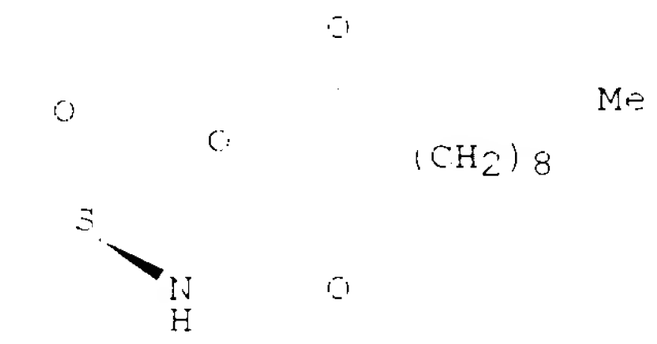
AB A method of cleaning or protecting surfaces by treatment with compns. comprising N-(**3-oxododecanoyl**)-L-homoserine lactone (oxoDHL) blocking compds. and/or N-butyryl-L-homoserine lactone (BHL) analogs, either in combination or sep. An example is given to det. the role of homoserine lactone signal mols. in the formation of biofilms by cells of Pseudomonas aeruginosa. A liq. general purpose heavy duty cleaner contained Calsuds 81N conc. 2.0-4.0, tetra-K pyrophosphate 5.0-10.0, Na xylenesulfonate (40%) 7.5-12.5, BHL analog 2.5 ppm and water to 100%.

IT **168982-69-2**, N-(**3-Oxododecanoyl**)-L-homoserine lactone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blockers; compns. for controlling biofilm development contg. homoserine lactone derivs.)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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REFERENCE(S): (1) Kramer; US 5320805 A 1994 CAPLUS

L7 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:456192 CAPLUS
DOCUMENT NUMBER: 129:198983
TITLE: Induction of entry into the stationary growth phase in Pseudomonas aeruginosa by N-acylhomoserine lactone
AUTHOR(S): You, Zhiying; Fukushima, Jun; Tanaka, Kan; Kawamoto, Susumu; Okuda, Kenji
CORPORATE SOURCE: Dep. Bacteriology, Yokohama City Univ. Sch. Med., Kanazawa-ku, Yokohama, 236, Japan
SOURCE: FEMS Microbiol. Lett. (1998), 164(1), 99-106
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-acylhomoserine lactone (AHSL, autoinducer) is capable of regulating a set of genes by sensing cell d. and developing an intercellular communication in Pseudomonas aeruginosa. Addn. of AHSL in the exponential growth phase, regardless of cell d., induces a repression of cell growth of P. aeruginosa, an expression of stationary phase specific factor .sigma.s in vivo and a morphol. change into smaller spherical shape indistinguishable from that in the stationary phase. It is demonstrated

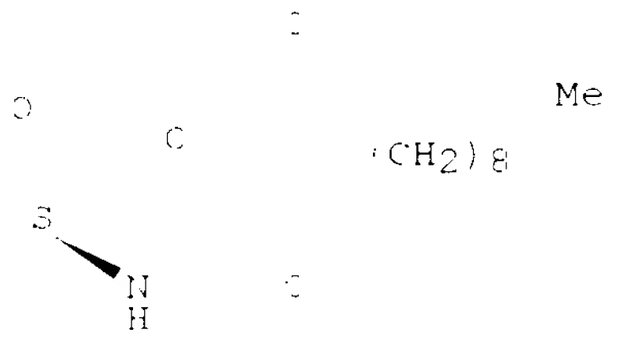
that AHSL can trigger an entry of bacteria into stationary phase as a growth controlling signal.

IT **168982-69-2**, N-(**Oxododecanoyl**)-L-homoserine lactone
RL: ESU (Biological study, unclassified); BIOL (Biological study)
(induction of entry into stationary growth phase in Pseudomonas aeruginosa by N-acylhomoserine lactone)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:397236 CAPLUS

DOCUMENT NUMBER: 129:131845

TITLE: Construction and analysis of luxCDABE-based plasmid sensors for investigating N-acyl homoserine lactone-mediated quorum sensing

AUTHOR(S): Winson, Michael K.; Swift, Simon; Fish, Leigh; Throup, John P.; Jorgensen, Frieda; Chhabra, Siri Ram; Bycroft, Barrie W.; Williams, Paul; Stewart, Gordon S. A. B.

CORPORATE SOURCE: Division of Food Sciences, School of Biological Sciences, Food Microbiology Section, University of Nottingham, Nottingham, Leics., LE12 5RD, UK

SOURCE: FEMS Microbiol. Lett. (1998), 163(2), 185-192
CODEN: FMLED7; ISSN: 0378-1097

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

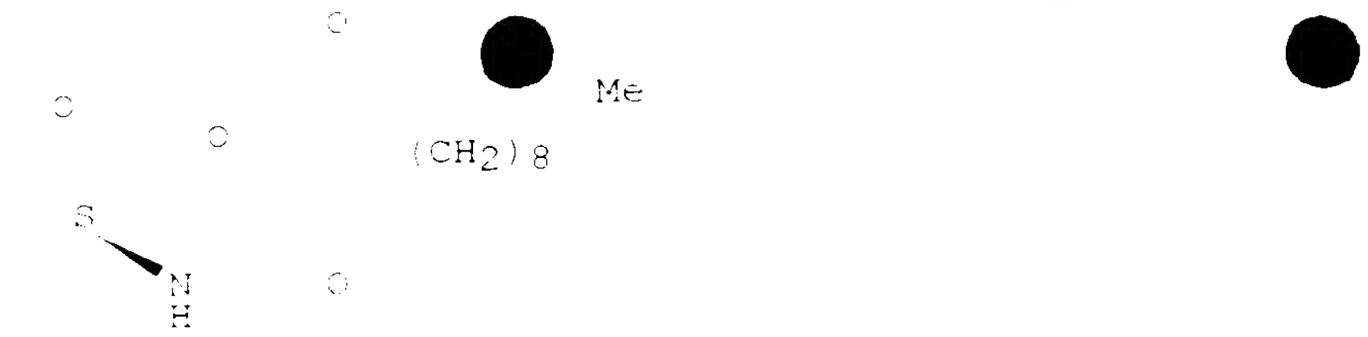
AB Plasmid reporter vectors have been constructed which respond to activation of LuxR and its homologs LasR and RhlR (VsmR) by N-acyl homoserine lactones (AHLs). The expression of luxCDABE from transcriptional fusions to PluxI, PlasI and PrhlI resp., occurs in the presence of activating AHLs. A profile of structure/activity relationships is seen where the natural ligand is most potent. The characterization of individual LuxR homolog/AHL combinations allows a comprehensive evaluation of quorum sensing signals from a test organism.

IT **168982-69-2**, N-3-(**Oxododecanoyl**)-L-homoserine lactone
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); ANST (Analytical study); BIOL (Biological study)
(construction and anal. of luxCDABE-based plasmid sensors for investigating N-acyl homoserine lactone-mediated quorum sensing)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:7602 CAPLUS
DOCUMENT NUMBER: 128:113981
TITLE: The Pseudomonas aeruginosa quorum-sensing signal molecule N-(**3-oxododecanoyl**)-L-homoserine lactone has immunomodulatory activity
AUTHOR(S): Telford, Gary; Wheeler, D.; Williams, Paul; Tomkins, P. T.; Appleby, P.; Sewell, Herbert; Stewart, Gordon S. A. B.; Bycroft, Barrie W.; Pritchard, David I.
CORPORATE SOURCE: Department of Life Science, University of Nottingham, University Park, Nottingham, NG7 2RD, UK
SOURCE: Infect. Immun. (1998), 66(1), 36-42
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

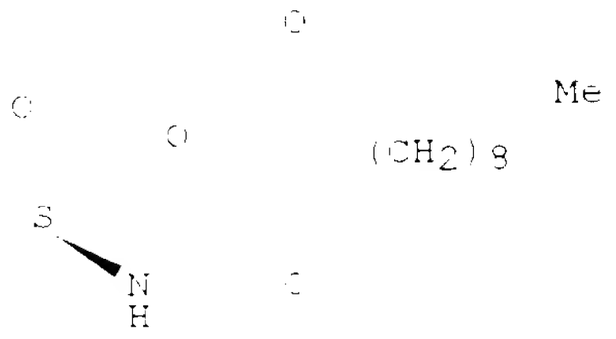
AB Diverse gram-neg. bacterial cells communicate with each other by using diffusible N-acyl homoserine lactone (AHL) signal mols. to coordinate gene expression with cell population d. Accumulation of AHLs above a threshold concn. renders the population "quorate," and the appropriate target gene is activated. In pathogenic bacteria, such as P. aeruginosa, AHL-mediated quorum sensing is involved in the regulation of multiple virulence determinants. The authors therefore sought to det. whether the immune system is capable of responding to these bacterial signal mols. Consequently the immunomodulatory properties of the AHLs N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL) and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL) were evaluated in murine and human leukocyte immunoassays in vitro. OdDHL, but not OHHL, inhibited lymphocyte proliferation and tumor necrosis factor .alpha. prodn. by lipopolysaccharide-stimulated macrophages. Furthermore, OdDHL simultaneously and potently down-regulated the prodn. of IL-12, a Th1-supportive cytokine. At high concns. (>7.times.10-5 M) OdDHL inhibited antibody prodn. by keyhole limpet hemocyanin-stimulated spleen cells, but at lower concns. (<7.times.10-5 M), antibody prodn. was stimulated, apparently by increasing the proportion of the IgG1 isotype. OdDHL also promoted IgE prodn. by interleukin-4-stimulated human peripheral blood mononuclear cells. Thus, OdDHL may influence the Th1-Th2 balance in the infected host and, in addn. to regulating the expression of virulence determinants, OdDHL may contribute to the pathogenesis of P. aeruginosa infections by functioning as a virulence determinant per se.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(Pseudomonas aeruginosa quorum-sensing signal mol. L-homoserine lactone has immunomodulatory activity)

RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX

NAME

Absolute stereochemistry.



L7 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:7770 CAPLUS
DOCUMENT NUMBER: 128:138160
TITLE: Quorum sensing and Chromobacterium violaceum: exploitation of violacein production and inhibition for the detection of N-acylhomoserine lactones
AUTHOR(S): Mcclean, Kay H.; Winson, Michael K.; Fish, Leigh; Taylor, Adrian; Chhabra, Siri Ram; Camara, Miguel; Daykin, Mavis; Lamb, John H.; Swift, Simon; Bycroft, Barrie W.; Stewart, Gordon S. A. B.; Williams, Paul
CORPORATE SOURCE: Department of Applied Biochemistry and Food Science, University of Nottingham, Loughborough, LE12 5RD, UK
SOURCE: Microbiology (Reading, U. K.) (1997), 143(12), 3703-3711
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quorum sensing relies upon the interaction of a diffusible signal mol. with a transcriptional activator protein to couple gene expression with cell population d. In Gram-neg. bacteria, such signal mols. are usually N-acylhomoserine lactones (AHLs) which differ in the structure of their N-acyl side chains. Chromobacterium violaceum, a Gram-neg. bacterium commonly found in soil and water, produces the characteristic purple pigment violacein. Previously the authors described a violacein-neg., mini-Tn5 mutant of C. violaceum (CV026) in which pigment prodn. can be restored by incubation with supernatants from the wild-type strain. To develop this mutant as a general biosensor for AHLs, the natural C. violaceum AHL mol. was first chem. characterized. By using solvent extn., HPLC and mass spectrometry, a single AHL, N-hexanoyl-L-homoserine lactone (HHL), was identified in wild-type C. violaceum culture supernatants which was absent from CV026. Since the prodn. of violacein constitutes a simple assay for the detection of AHLs, we explored the ability of CV026 to respond to a series of synthetic AHL and N-acylhomocysteine thiolactone (AHT) analogs. In CV026, violacein is inducible by all the AHL and AHT compds. evaluated with N-acyl side chains from C4 to C8 in length, with varying degrees of sensitivity. Although AHL compds. with N-acyl side chains from C10 to C14 are unable to induce violacein prodn., if an activating AHL (e.g. HHL) is incorporated into the agar, these long-chain AHLs can be detected by their ability to inhibit violacein prodn. The versatility of CV026 in facilitating detection of AHL mixts. extd. from culture supernatants and sepd. by thin-layer chromatog. is also demonstrated. These simple bioassays employing CV026 thus greatly extend the ability to detect a wide spectrum of AHL signal mols.

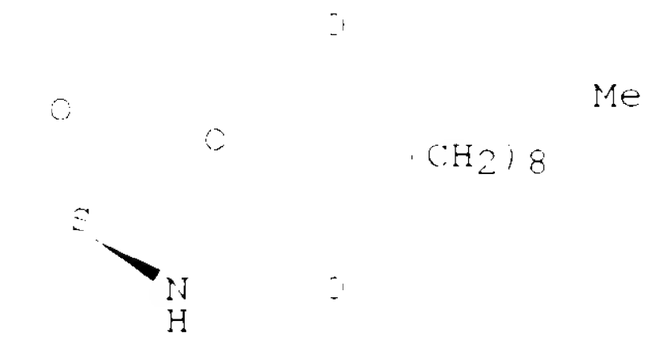
IT **168982-69-2**, n-(**3-Oxododecanoyl**) L-Homoserine lactone
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse ;

PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(quorum sensing and Chromobacterium violaceum exploitation of violacein prodn. and inhibition for the detection of acylhomoserine lactones)

RN 168982-63-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:625337 CAPLUS

DOCUMENT NUMBER: 127:303989

TITLE: Roles of Pseudomonas aeruginosa las and rhl quorum-sensing systems in control of elastase and rhamnolipid biosynthesis genes

AUTHOR(S): Pearson, James P.; Pesci, Everett C.; Iglewski, Barbara H.

CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, Rochester, NY, 14642, USA

SOURCE: J. Bacteriol. (1997), 179(18), 5756-5767
CODEN: JOBAAY; ISSN: 0021-9193

PUBLISHER: American Society for Microbiology

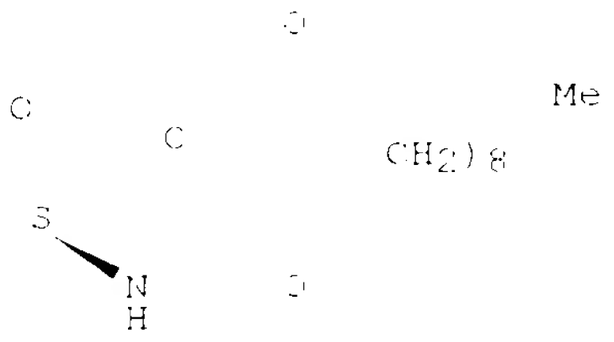
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two quorum-sensing systems (las and rhl) regulate virulence gene expression in Pseudomonas aeruginosa. The las system consists of a transcriptional activator, LasR, and LasI, which directs the synthesis of the autoinducer N-(**3-oxododecanoyl**)homoserine lactone (PAI-1). Induction of lasB (encoding elastase) and other virulence genes requires LasR and PAI-1. The rhl system consists of a putative transcriptional activator, RhlR, and RhlI, which directs the synthesis of N-butyryl homoserine lactone (PAI-2). Rhamnolipid prodn. in P. aeruginosa has been reported to require both the rhl system and rhlAB (encoding a rhamnosyltransferase). Here we report the generation of a .DELTA.lasI mutant and both .DELTA.lasI .DELTA.rhlI and .DELTA.lasR rhlR.DELTA.Tn501 double mutants of strain PAO1. Rhamnolipid prodn. and elastolysis were reduced in the .DELTA.lasI single mutant and abolished in the double-mutant strains. RhlAB mRNA was not detected in these strains at mid-logarithmic phase but was abundant in the parental strain. Further RNA anal. of the wild-type strain revealed that rhlAB is organized as an operon. The rhlAB transcriptional start was mapped, and putative .sigma.54 and .sigma.70 promoters were identified upstream. To define components required for rhlAB expression, we developed a bioassay in Escherichia coli and demonstrated that PAI-2 and RhlR are required and sufficient for expression of rhlA. To characterize the putative interaction between PAI-2 and RhlR, we demonstrated that [3H]PAI-2 binds to E. coli cells expressing RhlR and not to those expressing LasR. Finally, the specificity of the las and rhl systems was examd. in E. coli bioassays. The las system was capable of mildly activating rhlA, and similarly, the rhl system partly activated lasB. However, these effects were much less than the activation of rhlA by the rhl system and lasB by

the las system. The results presented here further characterize the roles
of the rhl and las quorum-sensing systems in virulence gene expression.
IT **168982-69-2**, N-(**3-Oxododecanoyl**) homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BPR Biological
process); MFM (Metabolic formation); BIOL (Biological study); FORM
(Formation, nonpreparative); PROC (Process)
(PAI-1; Pseudomonas aeruginosa las and rhl quorum-sensing systems in control of elastase and rhamnolipid biosynthesis genes)
RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:442322 CAPLUS
DOCUMENT NUMBER: 127:173757
TITLE: Regulation of the xcp secretion pathway by multiple quorum-sensing modulons in Pseudomonas aeruginosa
AUTHOR(S): Chapon-Herve, Virginie; Akrim, Mohammed; Latifi, Amel;
Williams, Paul; Lazdunski, Andree; Bally, Marc
CORPORATE SOURCE: Laboratoire d'Ingenierie des Systemes Macromoleculaires, Centre National de la Recherche Scientifique, Marseille, 13402, Fr.
SOURCE: Mol. Microbiol. (1997), 24(6), 1169-1178
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The virulence of the opportunistic pathogen Pseudomonas aeruginosa is largely dependent upon the extracellular prodn. of a no. of secreted proteins with toxic or degradative activities. The synthesis of several exoenzymes is controlled in a cell-d.-dependent manner by two interlinked quorum-sensing systems. Their secretion across the outer membrane occurs through the Xcp translocation machinery. The xcp locus located at 40 min on the chromosome consists of two divergently transcribed operons, namely xcpP-Q and xcpR to xcpZ. In this study, transcriptional fusions were constructed between the xcpP and xcpR genes and the lacZ reporter. Transcriptional activation of the xcpP and xcpR genes in P. aeruginosa is growth-phase dependent and the lasR-lasI auto-induction system is required
for this control. In the heterologous host Escherichia coli, the lasR gene product, together with its cognate autoinducer N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL), activates both the xcpP-lacZ and the xcpR-lacZ gene fusion. The second P. aeruginosa quorum-sensing modulon rhlR-rhlI (vsmR-vsmI) is also involved in the control of the xcp genes. Expression of the lacZ fusions is strongly reduced in PAN067, a pleiotropic mutant defective in the prodn. of N-acyl-homoserine lactones responsible for the activation of RhlR. Furthermore, introduction of the lasR mutation in PAN067 results in additional

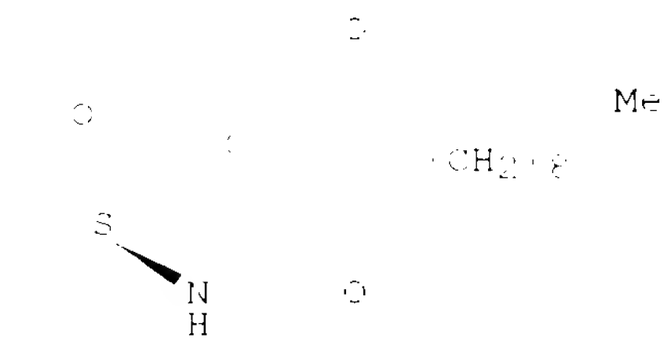
diminution of xcpR transcription, indicating that the two systems can regulate their target genes independently. These data demonstrate that expression of the xcp secretion system depends on a complex regulatory network involving cell-cell signaling which controls prodn. and secretion of virulence-assocd. factors.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(regulation of the xcp secretion pathway by multiple quorum-sensing modulons in Pseudomonas aeruginosa)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:49297 CAPLUS
DOCUMENT NUMBER: 126:155048
TITLE: Autoinducer molecule
INVENTOR(S): Pearson, James P.; Gray, Kendall M.; Passador, Luciano; Tucker, Kenneth D.; Eberhard, Anatol; Iglewski, Barbara H.; Greenberg, Everett P.
PATENT ASSIGNEE(S): The University of Iowa Research Foundation, USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5591872	A	19970107	US 1993-104487	19930809
US 6057388	A	20000502	US 1995-456864	19950601
PRIORITY APPLN. INFO.:			US 1993-104487	19930809

OTHER SOURCE(S): MARPAT 126:155048

AB Autoinducer mols., e.g., N-(**3-oxododecanoyl**)homoserine lactone, for Pseudomonas aeruginosa are described. The mols. regulate gene expression in the bacterium. Therapeutic compns. and therapeutic methods involving analogs and/or inhibitors of the autoinducer mols. also are described. The mols. are useful for treating or preventing infection by Pseudomonas aeruginosa.

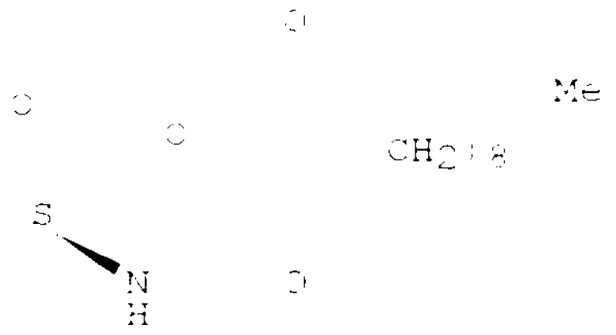
IT **168982-69-2P**, N-(**3-Oxododecanoyl**)homoserine lactone
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(autoinducer of Pseudomonas aeruginosa useful for preventing infection by Pseudomonas aeruginosa)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX

NAME:

Absolute stereochemistry.



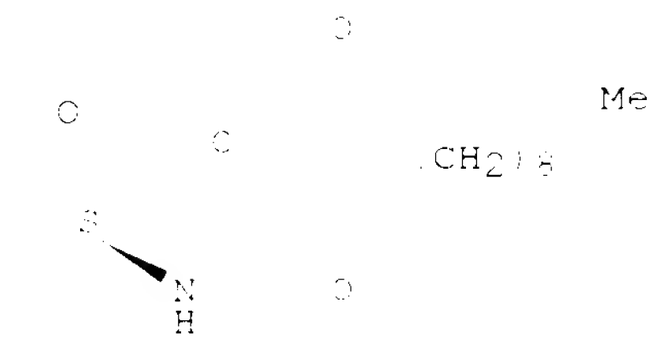
L7 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:43967 CAPLUS
DOCUMENT NUMBER: 126:153566
TITLE: Dissection of the promoter/operator region and evaluation of N-acylhomoserine lactone mediated transcriptional regulation of elastase expression in Pseudomonas aeruginosa
AUTHOR(S): Fukushima, Jun; Ishiwata, Tetsuyoshi; You, Zhiying; Ishii, Toshinori; Shigematsu, Takashi; Kurata, Minoru; Chikumaru-Fujita, Shizuko; Bycroft, Barrie W.; Stewart, Gordon S. A. B.; Kawamoto, Osumu; Morihara, Kazuyuki; Williams, Paul; Okuda, Kenji
CORPORATE SOURCE: Department of Bacteriology, Yokohama City University School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama, 236, Japan
SOURCE: FEMS Microbiol. Lett. (1997), 146(2), 311-318
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In Pseudomonas aeruginosa, expression of the lasB gene which codes for the metallopprotease, elastase, depends on small diffusible N-acylhomoserine lactones. LasB expression is regulated through the interactions of N-**3-oxododecanoyl**-L-homoserine lactone and N-butanoyl-L-homoserine lactone with the transcriptional activators LasR and VsmR(RhlR), resp. To investigate lasB expression further, the transcriptional start site was first located to a position 141 bp upstream from the translational start site. Using this information, a series of plasmids were constructed contg. consecutive 5' deletions of the upstream region of lasB fused to a promoterless chloramphenicol acetyltransferase reporter gene. The results obtained indicate that 3 regions are required for efficient transcription of lasB; a 35-bp palindromic sequence located at +26 to +60 bp upstream from the translation start site, and 2 regions located upstream of the transcription start site, at -135 to -55 bp and -65 to -26 bp, resp. Deletion of the latter region results in the loss of both N-butanoyl-L-homoserine lactone- and N-**3-oxododecanoyl**-L-homoserine lactone-mediated stimulation of lasB expression and provides further support for the role of this operator site as a target for either or both LasR and VsmR.

IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(dissection of the promoter/operator region and evaluation of N-acylhomoserine lactone mediated transcriptional regulation of elastase expression in Pseudomonas aeruginosa)

RN 168982-69-2 CAPLUS
CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



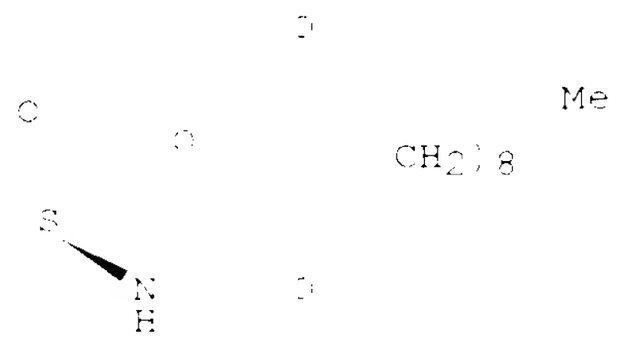
L7 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:606154 CAPLUS
DOCUMENT NUMBER: 125:267351
TITLE: A hierarchical quorum-sensing cascade in Pseudomonas aeruginosa links the transcriptional activators LasR and RhlR (VsmR) to expression of the stationary-phase sigma factor RpoS
AUTHOR(S): Latifi, A.; Foglino, M.; Tanaka, K.; Williams, P.; Lazdunski, A.
CORPORATE SOURCE: Lab. d'Ingenierie Dynamique Systemes Membranaires, Centre Natl Recherche, Marseille, 13402, Fr.
SOURCE: Mol. Microbiol. (1996), 21(6), 1137-1146
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Pseudomonas aeruginosa, the prodn. of many virulence factors and secondary metabolites is regulated in concert with cell d. through quorum sensing. Two quorum-sensing regulons have been identified in which the LuxR homologs LasR and RhlR are activated by N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL) and N-butanoyl-L-homoserine lactone (BHL) resp. The lasR and rhlR genes are linked to the luxI homologs lasI and rhlI, which are responsible for synthesis of OdDHL and BHL, resp. As lasRI and rhlRI are both involved in regulating synthesis of exoenzymes such as elastase, the authors sought to det. the nature of their interrelationship. By using lacZ transcriptional fusions in both homologous (P. aeruginosa) and heterologous (Escherichia coli) genetic backgrounds the authors provide evidence that (i) lasR is expressed constitutively throughout the growth cycle, (ii) rhlR expression is regulated by LasR.OdDHL, and (iii) that RhlR/BHL regulates rhlI. The authors also show that expression of the stationary-phase sigma factor gene rpoS is abolished in a P. aeruginosa lasR mutant and in the pleiotropic BHL-neg. mutant PAN067. Furthermore, the data reveal that in E. coli, an rpoS-lacZ fusion is regulated directly by RhlR/BHL. Taken together, these results indicate that P. aeruginosa employs a multilayered hierarchical quorum-sensing cascade involving RhlR/BHL and LasR/OdDHL, interlinked via RpoS, to integrate the regulation of virulence determinants and secondary metabolites with adaptation and survival in the stationary phase.
IT **168982-69-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(a hierarchical quorum-sensing cascade in Pseudomonas aeruginosa links

the transcriptional activators LasR and PhlR (VsmR) to expression of the stationary-phase sigma factor RpoS)

RN 168982-69-2 CAPLUS

CN Dodecanamide, 3-oxo-N-[(3S)-tetrahydro-2-oxo-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L? ANSWER 21 OF 21 CAPLUS COPYRIGHT 2010 ACS

ACCESSION NUMBER: 1995:841696 CAPLUS

DOCUMENT NUMBER: 123:256083

TITLE: Multiple N-acyl-L-homoserine lactone signal molecules regulate production of virulence determinants and secondary metabolites in Pseudomonas aeruginosa

AUTHOR(S): Winson, Michael K.; Camara, Miguel; Latifi, Amel; Foglino, Maryline; Chhabra, Siri Ram; Daykin, Mavis; Bally, Marc; Chapon, Virginie; Salmond, George P. C.; et al.

CORPORATE SOURCE: Dep. Applied Biochemistry and Food Science, Univ. Nottingham, Leicestershire, LE12 5RD, UK

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(20), 9427-31
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB P. aeruginosa produces a spectrum of exoproducts, many of which have been implicated in the pathogenesis of human infection. Expression of some of these factors requires cell-cell communication involving the interaction of a small diffusible mol., an autoinducer, with a pos. transcriptional activator. In P. aeruginosa PAO1, LasI directs the synthesis of the autoinducer N-(**3-oxododecanoyl**)-L-homoserine lactone (OdDHL), which activates the pos. transcriptional activator, LasR. Recently, a 2nd signaling mol.-based modulon in PAO1, termed vsm, was discovered, which contains the genes vsmR and vsmI. Using HPLC, mass spectrometry, and NMR spectroscopy it was here established that in Escherichia coli, VsmI directs the synthesis of N-butanoyl-L-homoserine lactone (I) and N-hexanoyl-L-homoserine lactone (II). These compds. are present in the spent culture supernatants of P. aeruginosa in a molar ratio of .apprxeq.10:1 and their structures were unequivocally confirmed by chem. synthesis. Addn. of either I or II to PAO67, a pleiotropic P. aeruginosa mutant unable to synthesize either of these autoinducers, restored elastase, chitinase, and CN- prodn. In E. coli carrying a VsmR 'vsmI'::lux transcriptional fusion, I and II activated VsmR to a similar extent. Analogs of these N-acyl-L-homoserine lactones in which the N-acyl side chain has been extended and/or oxidized at the C-3 position exhibit substantially lower activity (e.g., OdDHL) or no activity (e.g., dDHL) in this lux reporter assay. These data indicate that multiple families of quorum-sensing modulons interactively regulate gene expression in P. aeruginosa.

IT **168982-69-2**

RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(structure-activity relations in acylhomoserine lactone-mediated

activation of transcription factor VsmR)

RN 168982-69-2 CA[redacted]US

CN Dodecanamide, [redacted]xo-N-[(3S)-tetrahydro-2-oxo-3-[redacted]xanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.